Clinical Medicine

Original Articles for September, 1958

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• DEPRESSION • LOSS OF MEMOR
• INABILITY TO CONCENTRA

NOTE: No side effects are observed save for occasional and tran
"niacin flush" in sensitive individuals.

1. Boernstein, W. S.: Tr. New York Acad. Sci. *20*:72, 1957.

ADDITIONAL REFERENCES: Smigel, J. O.: M. T
85:149, 1957; Levy, S.: J.A.M.A. *153*:1260, 1953; Thompson,
and Procter, R. C.: North Carolina M. J. *15*:596, 1954; B
H. J.: Missouri Med. *53*:1071, 1956.

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EDITORIAL

On the Use and Abuse of Tranquilizing Drugs

Facts concerning the four general groups of these agents that should promote more discretion and greater discrimination in their use

JAMES M. NORTHINGTON, M.D., *Editor*

All peoples in all ages have sought nepenthe. Opium, hashish, coca leaves, tobacco, alcohol—one or more of them has strong appeal to the vast majority of humankind. Solomon adjures (Proverbs 31:6,7), "Give wine unto those that be of heavy hearts. Let him drink and forget his poverty, and remember his misery no more." Of a wealthy kinsman of mine it used to be said when he went on a spree, "He has either made a killing on Wall Street and is celebrating, or he has lost heavily and is drowning his sorrow."

Whatever may be the explanation, we are confronted with the fact that "tranquilizers" are extremely potent drugs, and that they are now being sold by the millions-of-dollars worth in this country. Following the long-established rule, "a drug potent for good is also potent for evil," every doctor should learn all there is to be known about these "tranquilizers."

A comprehensive study dealing with this matter by Hollister[1] forms the basis of this editorial.

By "tranquilizers" is meant drugs capable of causing sedation without impairing consciousness. It is claimed for them that they have revolutionized the treatment of patients in mental hospitals. The number of these drugs is increasing at a terrific rate and the same compound appears under many trade-names. Many of

1. Hollister, L. E., *California Med.*, 89:1-6,1958.

these drugs have a variety of actions, the relative importance of which is still not established.

Most tranquilizing drugs fall into one of four general groups, according to chemical structure:

1. Phenothiazine derivatives.
2. Rauwolfia alkaloids.
3. Substituted propane- or butanediols.
4. Diphenylmethane derivatives.

For the most part, drugs within each group have similar clinical indications and disadvantages.

PHENOTHIAZINE DERIVATIVES

These are currently most used and of greatest research interest. The sedative effects, so different from those of older sedatives as to warrant the use of the epithet "tranquilizing," are well known. Chlorpromazine and its congeners calm without impairing motor function or enforcing sleep. They regulate the intensity with which stimuli are appreciated and the emotional reactions evoked. Much of the emotional response to external or internal stimuli would be diminished by such action.

Chlorpromazine potentiates analgesic and anesthetic agents to a moderate degree, and has been used in surgical anesthesia and in treating painful states such as metastatic malignant disease. Some derivatives are drugs of choice in treating nausea and hiccough.

Virtually every psychiatric syndrome has been treated, usually with benefit, by chlorpromazine. Particularly important has been its ameliorating effect on schizophrenic reactions. It is now the standard against which all succeeding psychotherapeutic drugs must be measured. Some of the other phenothiazines, *e.g.*, the piperazine derivatives or the fluorinated compounds, have tranquilizing properties equal to or superior to chlorpromazine. Some, *e.g.*, prochlorperazine, may be better antiemetics. However, chlorpromazine, promazine, and triflupromazine, still are more useful in potentiating other drugs.

Chlorpromazine may bring about two serious complications: Jaundice occurs in fewer than 2 per cent of patients treated for more than a week, and agranulocytosis has occurred with promazine, triflupromazine and mepazine—not yet from the piperazine derivatives. Adrenergic blocking effects, which have led to severe hypotensive crises in some patients treated with chlorpromazine, appear to be less with the newer drugs. On the other hand, the piperazine derivatives produce more severe extrapyramidal signs. In addition to the usual triad of muscle rigidity, resting tremor and loss of associated movements, states of uncontrolled motor activity, oculogyric crises and spasms of the neck, tongue and pharyngeal muscles are frequently encountered. These manifestations are rare except from the high doses used in psychiatric treatment.

RAUWOLFIA ALKALOIDS

By an odd coincidence, extracts of the ancient plant Rauwolfia were introduced to Western medicine almost simultaneously with the increased interest in phenothiazine derivatives. Originally studied for their effects on arterial hypertension, an incidental observation led to their use as tranquilizing agents. Of 36 alkaloids found in the plant, three pure alkaloids, reserpine, rescinnamine and deserpidine, are in clinical use. The chemical differences are slight, as are the pharmacologic differences.

The actions of the whole root extracts or the alseroxylon fraction of Rauwolfia are similar to those of the pure alkaloids. Reserpine has been most widely used.

Unlike chlorpromazine, reserpine stimulates the reticular activating system rather than depressing it. For this reason, reserpine is not as powerful a sedative as chlorpromazine. On the other hand, reserpine stimulates the amygdaloid complex much as chlorpromazine does.

Tranquilization and antihypertensive action have been the main indications for the clinical use of the alkaloids. As with chlorpromazine, virtually every kind of psychiatric disorder, except mental depression, has been treated successfully with reserpine. Rauwolfia alkaloids aggravate existing depression and may produce it in patients not previously depressed. In severe psychiatric disorders, such as schizophrenic reactions, the phenothiazine derivatives appear to produce greater benefits, faster and in more patients. The minor side reactions of reserpine (stuffy nose, lethargy and muscle aching) have made other tranquilizers (*e.g.*, meprobamate) preferable for treating emotional disorders of the milder types.

The Rauwolfia alkaloids remain the basic drugs in the treatment of hypertension. Early or mild hypertension can usually be managed solely with these drugs. Seldom is it necessary to give more than 2 mg. of reserpine daily, and maintenance doses may be as small as 0.25 mg. a day. Even severe hypertensive states may respond to large doses given parenterally. Management of severely hypertensive states over a long term requires combination of reserpine with hydralazine, pentolinium or chlorisondamine.

Mental depression occurs somewhat oftener in patients treated for hypertension than in psychotic patients. The large doses of reserpine used in psychiatric practice (usually in excess of 2 mg. daily) have been known to activate duodenal ulcers, sometimes with hemorrhage. This danger is less when hypertension is being treated. Nevertheless, close attention should be paid to ulcer management when such patients receive Rauwolfia alkaloids. Rescinnamine and deserpidine might be preferable for some patients.

SUBSTITUTED PROPANEDIOLS OR BUTANEDIOLS

These two drugs were developed originally to improve the skeletal muscle relaxant properties of mephenesin. Meprobamate, the most widely used of this group, seems to have more sedative effect. It has been used chiefly for treating temporary anxiety in "normal" persons and more severe and chronic anxiety in the psychoneurotic. Whether or not it is superior to barbiturates is a question. Barbiturates are to be preferred for treating insomnia. Allergic reactions, often to the first dose of meprobamate, are the most frequent complication. Withdrawal reactions may follow abrupt discontinuance. As with barbiturates, the taking of large quantities of this drug along with alcohol may be fatal.

DIPHENYLMETHANE DERIVATIVES

Hydroxyzine, a sedative and a potent antihistaminic, is used in treating milder emotional disorders and skin disorders. Because of its low toxicity, it is being increasingly used as a sedative. Benactyzine is said to be useful in treating psychoneuroses, especially phobia and compulsion. Pi-

pradrol is a mild stimulant. Isopropamide is a rather long-acting and potent anticholinergic.

DISCUSSION

The rapid evolution of tranquilizers is in part a reflection of a widespread need for comfort in an "age of anxiety." Appreciation of mental illness as one of the costliest of human afflictions has had its influence. The fact that chemical agents may ameliorate schizophrenic reactions has engendered some hope for the solution of this problem.

These drugs have been greatly abused. An honest doctor must do what is good for the patient, not what is most expedient. For some patients, a tolerable amount of anxiety which leads to problem-solving is far better than a temporary though pleasant relief. The tranquilizing drugs should be used when anxiety becomes disabling, and then only when coupled with efforts to find and remove the source of anxiety. While the taking of tranquilizers might be preferable to a rising tide of alcoholism or narcotic drug addiction, it should not be encouraged as a national practice. Many severely psychotic patients have been considerably helped by these drugs, especially the phenothiazines and the Rauwolfia alkaloids. For acutely ill patients the course of illness may be shortened, permitting a briefer period in the hospital. Many chronically psychotic patients who seemed doomed to a lifetime in mental hospitals are now able to live outside. Mental hospitals have accelerated efforts to become treatment centers rather than custodial institutions. Tranquilizing drugs have provided some measure of hope for these patients.

Fortunately, we have neither to know the cause of the disease nor the way a treatment works in order to apply it to the good of our patients.◀

A New Common-Duct Scoop

Before closing the common duct after choledochostomy the surgeon must demonstrate that there is no obstruction of the distal end of the duct. Easy passage of a 3-mm. dilator establishes this. However, all surgeons have probably experienced extreme difficulty in passing a probe dilator or scoop through the sphincter of Oddi, even when that structure is normal. The common duct is easily damaged, and extreme care and gentleness are required in instrumental exploration. In difficult cases the surgeon is confronted with two alternatives—desisting short of a complete exploration, or exerting a little more pressure and possibly making a false passage with accompanying leakage and damage to adjacent structures.

The basic principle of a new scoop for such exploration is borrowed from urology. This scoop differs from the usual common-duct scoops in two respects. The leading edge has a threaded projection and is designed to accept a detachable, woven filiform of size 4 French with standard 1/56 thread. The second difference is the gradualness of the narrowing from scoop to shaft, which eliminates a shoulder that might hinder withdrawal of the scoop.

This instrument has been useful in safely completing satisfactory exploration of the distal common duct, and in engaging and removing impacted stones in this region.

Ferris, D. O., *Proc. Staff Meet. Mayo Clin.*, 33:117-118,1958.

ORIGINAL ARTICLE

A Pharmacological Basis for General Anesthesia

Careful coordination of premedicants and general anesthetics, with individualized dosage and precise techniques, are recommended

D. LEROY CRANDELL, M.D., *Winston-Salem, North Carolina*

With the ever increasing number of drugs used to induce and maintain general anesthesia, only adherence to basic pharmacological principles can avert an increase in anesthetic morbidity and mortality. As a clinical pharmacologist, the modern anesthesiologist administers a combination of drugs to produce general anesthesia. This has proven safer than using a single agent. Of course it is literally polypharmacy, since Gr. *poly* means many, and Gr. *pharmakon* means drug. But it is not polypharmacy of the kind to be condemned, if strict conformity to basic pharmacological principles is maintained.

The preanesthetic medication and the anesthetic medication must be coordinated to complement each other. The primary objective of preanesthetic medication is psychic sedation and parasympatholysis, without cardiovascular and respiratory depression.

The selection and dosage of the premedicant must be individualized to conform with fundamental pharmacological principles. The physical status and metabolic activity of the patient determines the dose required to produce an optimum effect. Too often, drugs are administered according to average doses. Many patients are not "average" and the result is inadequate sedation or depression of vital mechanisms. Routine ordering of these drugs by persons unfamiliar with their actions in relation to the

anesthetic agents should be discouraged. Preanesthetic medication is to be given in the proper dose, by the proper route and at the proper time to exert its maximum effect just prior to the induction of anesthesia.

The traditional hypodermic injection of a narcotic and a belladonna derivative has resulted in unnecessary cardiovascular and respiratory depression. Unless the patient is in pain he needs no narcotic. Satisfactory sedation can be achieved by judicious use of a barbiturate. The short-acting barbiturates, such as pentobarbital and secobarbital, are preferred unless the patient has liver disease, in which case the long-acting barbiturates, such as barbital and phenobarbital, are preferred. The long-acting barbiturates are excreted mainly by the kidney and are not dependent on the liver for detoxification. The usual dose of a barbiturate administered before a local anesthetic will not prevent toxic reactions manifested by central nervous system stimulation. A dose of a barbiturate large enough to prevent convulsions will aggravate toxic reactions manifested by cardiovascular depression.

Undesirable responses of the psyche to the contemplated anesthesia and the operation can be partially prevented by the employment of certain therapeutic devices. The preanesthetic visit, by allaying apprehension, can increase the effectiveness of the drugs employed to produce sedation. Drugs are a poor substitute for understanding between patient and physician.

Patients who misinterpret touch, pressure and traction as pain while under regional, spinal, or local anesthesia are benefited by the intravenous administration of a narcotic.

The belladonna derivatives help dry up the secretions and reduce autonomic reflexes mediated through the vagus nerve. They should not be used before a spinal, local or regional anesthetic. Evidence is accumulating that larger doses of parasympatholytic drugs can be employed without deleterious effects. Scopolamine has the advantage over atropine in that it produces amnesia and has more antisecretory effect. Atropine has a more profound effect in preventing deleterious reflex cardiovascular disturbances mediated over the vagus nerve. Barbiturates and scopolamine produce excitement, restlessness and disorientation in patients with advanced cerebral arteriosclerosis. Chloral hydrate and atropine are a better choice for preanesthetic medication in such cases. Despite many enthusiastic reports on the tranquilizers as premedicants, the data to support this enthusiasm lack proper control. Extreme caution must be taken in using the tranquilizers in combination with depressant drugs.

ANESTHESIA MANAGEMENT

Safe anesthesia requires that the variety of controllable drugs available for use in anesthesia be used according to basic pharmacological principles. The anesthetic state can be divided into its three major components, hypnosis, analgesia and muscular relaxation. Drugs should be employed to produce each of these components for which its pharmacological properties are best suited. The choice of the anesthetic agent is based primarily on the physical status. There is a wide variation in the physical status of the surgical patient, hence an individualized regimen is required. The physical status is far more important than age.

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*Levine, A. J., et al.: Clinical Medicine 5:907 (July) 1958

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REFERENCES: Eichner, E.: Premenstrual Tension Syndrome (PTS), Scientific Exhibit, New York State Acad. General Practice, New York (Oct.) 1957 • Kalz, F., Scott, A.: A.M.A. Arch Dermatol. 74:493 (Nov.) 1956 • Morton, J. H.: The Prescriber 2:12 (Sept.) 1955 • Eichner, E., Waltner, C.: M. Times 83:771 (Aug.) 1955 • Morton, J. H.: Internat. Rec. Med. 166:505 (Nov.) 1953.

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HYPNOSIS

Thiopental and thiamylal are the thiobarbiturates most commonly used to produce hypnosis. Clinically there is no significant difference in their pharmacological effect. The classification of these drugs as intravenous anesthetics is a misnomer since they possess no analgesic properties unless profound physiologic depression is produced. They are the most abused drugs used in anesthesia. Due to their rapid plasma-tissue distribution they have been classified as ultra-short-acting barbiturates. However, their actual metabolic break-down is slow, amounting to about 10 to 15 per cent per hour.[1] Thus a prolonged recovery may result following the administration of large doses. They do not obtund or abolish laryngeal, tracheal or bronchial reflexes, unless such large doses are administered that subsequent profound physiologic depression occurs. The insufficient analgesia is responsible for the frequent occurrence of laryngospasm and bronchospasm. In the presence of an increased blood urea, bronchial asthma, cardiovascular disease, liver dysfunction hypovolemia, they should be used with extreme caution. Their administration can precipitate an attack of acute prophyria resulting in a lower-motor-neuron paralysis and even death.

The thiobarbiturates are valuable adjuncts to anesthesia, and their use should be restricted to producing basal hypnosis. To attempt to produce anesthesia with these agents is to deliberately induce a state of acute barbiturate poisoning. Recently central nervous system stimulants have been advocated to hasten recovery from so-called barbiturate anesthesia, and thus prevent certain postoperative complications. This only serves to foster further misuse of thiobarbiturates. It is not the solution to their improper administration.

ANALGESIA

Nitrous oxide is a weak anesthetic agent. It is the safest anesthetic available when used with adequate oxygen concentrations. To attain the maximal analgesic benefit from nitrous oxide, denitrogenation is necessary. When required, supplemental analgesia can be provided with diethyl ether, divinyl ether, cyclopropane, narcotics, trichlorethylene or fluothane. The use of the more potent anesthetic agents to supplement the analgesia of nitrous oxide will result in the use of lower concentrations and the reduction or elimination of adverse side-effects.

At the conclusion of anesthesia with nitrous oxide, the residual oxygen is diluted by the outward diffusion of nitrous oxide from the blood. This results in a decrease in the partial pressure of alveolar oxygen. This diffusion hypoxia can be prevented by providing a high oxygen concentration while nitrous oxide is being eliminated.

DIETHYL ETHER

The pharmacological action of ether is the combined result of direct depression and reflex sympathoadrenal release. The myocardial effect of ether is determined by the quantitative reflex release of epinephrine and norepinephrine from the adrenal medulla and sympathetic nerve endings. The direct myocardial or negative inotropic effect of ether upon the myocardium is antagonized by the

1. Dundee, J. W., Thiopentone and Other Thiobarbiturates, Edinburgh and London, E. & S. Livingstone, Ltd., 1956.

pos tive inotropic effect of epinephrine an norepinephrine.[2] The clinical signif ance of this myocardial effect is tha critical myocardial depression an profound hypotension may resu from the direct depressant effect of ther upon the myocardium. This occ irs when the reflex release of epi ephrine and norepinephrine from the adrenal medulla and sympathetic ner e endings is reduced or abolished. A iseased myocardium may show a dec eased response to the positive inotr pic effect of epinephrine and norepi ephrine.

I ther exerts a dual action on the me ullary respiratory center consisting of direct depression and reflex stimulation, the latter due largely to the stimulating effect of mobilized epinephrine, the sensitization of pulmonary stretch receptors and the stimulation of extrapulmonary sensory receptors.[3]

Prolongation of the recovery period predisposes the patient to pulmonary complications. This has resulted in the popular misconception of ether pneumonia. General debility associated with a protracted recovery and hypoventilation are not specific sequelae of ether anesthesia.

OLDER VIEWS NEED MODIFICATION

As a result of the improvements in anesthetic technics and biochemical investigation, many of the older views concerning the metabolic effects of ether need modification. Effects of ether on lower animals are not always transferable to man. The reflex sympathoadrenal release during ether anesthesia is responsible for the hyperglycemia and the subsequent acidosis. This metabolic effect of reflex sympathoadrenal release is suppressed by pentobarbital premedication, thiopental induction[4] and chemical sympathetic blockade.

Although other anesthetic agents may be more desirable in the diabetic patient, the primary concern in the management of the diabetic patient during surgery is to administer adequate insulin and glucose to maintain carbohydrate metabolism without the production of hypoglycemia or acidosis. Disturbances in acid-base equilibrium are in most instances the consequence of inadequate pulmonary ventilation. The type of anesthetic agent used is less important than its proper administration.

Experience indicates that anesthesia *per se* when conducted with ether does not seriously influence the course of hepatic and renal disease, unless the dosage is excessive and associated with hypoxia. A well conducted anesthesia, with the maintenance of adequate tissue oxygenation and perfusion, is more important than the effect of ether in preventing hepatic and renal damage.

Often it is stated that open-drop ether is the safest anesthetic. This is true only in the hands of the untrained anesthetist. If this technic is used, oxygen should be insufflated under the mask via catheter at a rate of one to two liters per minute. The absence of means to compensate respiration with this technic in order to maintain adequate alveolar ventilation is a definite disadvantage.[5]

There are certain factors which usually contribute to the so-called ether convulsion. A toxic child premedicated with atropine and anesthetized with open-drop ether, in the pre-

2. Brewster, W. R., Jr., et al., *Am. J. Physiol.*, 175: 399-414,1953.
3. Dripps, R. D., & Severinhaus, J. W., *Physiol. Rev.*, 35:741-777,1955.
4. Bass, W. P., et al., *Anesthesiology*, 14:18-22,1953.
5. Crandell, D. L., *North Carolina M.J.*, 18:497-504,1957.

sence of a high endogenous and exogenous temperature, has an elevation of the metabolic rate with a high carbon dioxide output which is inadequately eliminated, and a high oxygen demand which is inadequately supplied. Thus the stage is set for a convulsion.

CYCLOPROPANE

The tendency has been to blame this agent for the occurrence of cardiac arrhythmias during anesthesia and for the hypotension that follows. Respiratory acidosis is associated with a rise in the peripheral blood epinephrine, norepinephrine and potassium levels in the human. The sudden reduction of carbon dioxide tension at the conclusion of anesthesia will result in a further elevation of serum potassium, and subsequent hypotension cardiac arrythmias and even ventricular fibrillation may develop. Close attention to proper administration with prevention of overdose and maintenance of adequate alveolar ventilation will help to avert these complications. Cyclopropane appears to sensitize the myocardium to epinephrine. If a vasopressor is required during cyclopropane anesthesia, phenylephrine or methoxamine should be used.

There is no specific evidence that cyclopropane is contraindicated in patients with auricular fibrillation and ventricular or auricular premature contractions. In fact, these arrhythmias will often disappear during cyclopropane anesthesia. Nevertheless, a cautious approach with electrocardiographic monitoring is imperative when administering cyclopropane to a patient with an abnormality of the cardiac conduction system.

There is an apparent increase of bleeding with cyclopropane as compared with other agents. This oozing is confined to the skin and muscle and ceases on closure of the wound. The most probable cause is peripheral vasodilation, particularly of the vessels in the skin and muscle, and an elevation in the venous pressure. There is no significant alteration in the bleeding and clotting time. The bleeding is enhanced by inadequate pulmonary ventilation.

NARCOTICS

The narcotics such as meperidine, morphine, anileridine, levo-dromoran, and alphaprodine have been of value in supplementing the analgesic effect of nitrous oxide. The narcotic can be administered as a drip or in intermittent doses intravenously. Preanesthetic medication with a narcotic is of value in this instance. Toward the end of the anesthesia, the narcotic should be discontinued in order to avoid postoperative depression. The antinarcotics such as N-allynormorphine hydrochloride or levallorphan tartrate may be of use if over-depression is produced. These antinarcotics displace the narcotic from the receptor cells in the respiratory center. They are not respiratory stimulants, but actually replace a profound respiratory depression with a lesser degree of respiratory depression. With the enhanced ventilation and elimination of accumulated carbon dioxide, the respiratory center is re-sensitized to its normal physiological stimulus, carbon dioxide.

MUSCLE RELAXANTS

The neuromuscular blocking agents have greatly contributed to the safety of general anesthesia. Adequate muscular relaxation can be obtained without recourse to deep anesthesia. Thus the physiologic mechanisms

which compensate for trauma and acute blood loss are preserved. The neuromuscular blocking agents are indicated to provide muscular relaxation and to facilitate endotracheal intubation. All too frequently, muscle relaxants are used for surgical procedures in which muscle relaxation is not a requirement. The only danger from the muscle relaxants is in their misuse. They allow the novice to mask poorly administered anesthesia. The deleterious effects may not be evident until the postoperative period.

The depolarization-repolarization sequence mediated by the acetylcholine acetylcholinesterase system is essential for physiological neuromuscular transmission. The muscle relaxants produce neuromuscular blockade by interfering with either the depolarization or repolarization phase of neuromuscular transmission. Gallamine and d-tubocurarine exert their pharmacological effect by interfering with the depolarization phase. It was previously thought that succinylcholine produced a persistent depolarization and thus interfered with the repolarization phase. More recent evidence indicates that there is a mixed effect at the neuromuscular junction. The anticholinesterase effect of neostigmine and edrophonium, by interfering with the hydrolysis of acetylcholine, will restore neuromuscular transmission. The predominant action of edrophonium is cellular displacement with only a weak anticholinesterase action. This reversal of neuromuscular blockade is more effective with d-tubocurarine and gallamine.

DEPTH OF ANESTHESIA

The present-day technic of light surgical anesthesia plus a muscle relaxant allows the maintenance of a more nearly normal physiologic state of unconsciousness and pain relief, and minimizes the adverse effects on the respiratory and cardiovascular systems produced by deep surgical anesthesia. The detrimental effects of deep general anesthesia are analogous to those of high spinal anesthesia. The depth of anesthesia should be coordinated with the surgical requirements of the operation, and for this the anesthesiologist must possess a knowledge of the surgical procedure in order that he may anticipate the anesthetic requirements for each surgical maneuver.

CONCLUSION

In order to reduce anesthetic morbidity and mortality, it is essential that each drug employed be used for that purpose for which its pharmacologic properties are primarily suited.

The judgment and skill of the anesthesiologist are more significant than the anesthetic agent employed. In the past too much emphasis has been placed on individual agents in trying to explain the etiology of anesthetic complications. A patent airway, adequate tissue oxygenation and carbon dioxide elimination, accompanied by the application of sound physiologic and pharmacologic principles, are the basic requirements in the management of any patient during anesthesia and surgery. With the advent of medical anesthesia associated with improved biochemical investigational methods and more extensive research in anesthesia, many of the untoward side effects attributed to individual anesthetic agents have been shown to be directly related to faulty and improper administration.◀

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ORIGINAL ARTICLE

Oral Therapy in Respiratory Tract Disorders

The treatment of upper respiratory infections is simplified through the selective action of this new oral medication

DONALD F. FARMER, M.D., *Chicago, Illinois*

Nose drops, sprays and inhalers for "shrinking" the nasal mucosa are currently ameliorating the symptoms of the common cold to a gratifying degree.[1]

Neither patients nor doctors, however, are completely satisfied with locally applied shrinking agents, for their effect is limited to the relatively small area of the mucous lining of the respiratory tract which can be reached from the nostrils.[2-4,5] During a cold, a heavy discharge flushes away much of the vasoconstrictor, preventing contact with the inflamed membrane. Another shortcoming of topically applied agents is their propensity to cause rebound congestion and, on repeated use, damage to the nasal mucosa.[2,3,6]

Oral therapy appears to be effective not only in such conditions as nasal congestion and rhinorrhea, usually treated with topical nasal preparations, but also in numerous other respiratory disorders such as postnasal drip and chronic bronchitis. This report concerns the treatment of upper respiratory infections with an oral medication* containing an effec-

1. Hunnicutt, I. G., *Postgrad. Med.*, 20:625,1956.
2. Proctz, A. W., et al., *Tr. Am. Acad. Ophth.*, 58:533,1954.
3. Young, B. M., *J. Am. M. Women's A.*, 11:282, 1956.
4. McMahon, B. J., *Ann. Otol. Rhin. and Laryng.*, 64:230,1955.
5. Proctz, A. W., Essays On The Applied Physiology of The Nose, The Annals Publishing Co., St. Louis, 1941. p. 397.

**Triaminic®*, Each tablet contains Phenylpropanolamine hydrochloride, 50 mg.; Pheniromine maleate, 25 mg.; Pyrilamine maleate, 25 mg. Supplied by the Smith-Dorsey Division of The Wander Company, Lincoln, Nebraska.

6. Rising, J. D., *Missouri Med.*, 51:774,1954.

tive sympathomimetic amine and two antihistamines that exerts a decongestant and "normalizing" influence for several hours after each dose.[7] The excellent response obtained may be the result of thorough distribution of the active principles by the blood stream to all of the mucous membrane. This medication effectively controlled several respiratory tract disorders not amenable to relief with topical vasoconstrictor therapy. One of these disorders, the postnasal drip syndrome, is found in almost every section of the country[2,3,8,9] and has not yielded to any previous therapy.[10]

METHOD OF STUDY

A total of 189 patients were chosen at random to represent a wide range of respiratory problems involving allergy and congestion. Eleven symptom complexes were included, varying in severity and complexity from acute upper respiratory infection to bronchiectasis.

The medication used encloses a small tablet containing half of the total of each ingredient in the middle of the completed tablet. The outer covering releases its ingredients promptly after the tablet is swallowed, and the inner tablet's disintegration is delayed for approximately three hours. Decongestant and bronchodilator actions are exerted without producing apreciable central nervous system stimulation.[11] The antihistaminics reduce the rhinorrhea through their weak parasympatholytic action and may increase the resistance of the mucosa to infection.[12] The histamine antagonists also may produce benefit by combating the allergic factors which are frequent in respiratory disorders. Due to the construction of the tablet, half of the ingredients are released immediately to provide approximately three or four hours of relief, then the ingredients in the core continue the effect for a total of approximately six to eight hours.

The dosage used varied from one tablet daily to one table every four hours. In general, lower dosages were used in chronic cases, higher dosages were used in acute problems. When initial response was not satisfactory at the dosage level chosen, the number of tablets per day was increased until maximum benefit was obtained.

In the majority of cases the results were estimated in the office at the first visit after the drug was prescribed. The criteria for improvement included results of examination of the lung fields, confirmatory x-ray where indicated, transillumination of the sinuses and visual inspection of the nose, pharynx and throat. In the few instances where the patient could not be seen for follow-up, telephone reports were used.

RESULTS

The number of patients treated for any given symptom complex varied from 87 with acute upper respiratory infections to one each with recurrent tonsillitis and acute adenoiditis with myringitis. The results obtained are helpful in indicating the outer limit of usefulness of oral therapy for respiratory tract disorders. All symptoms were eliminated in 37 per cent of the cases, and 46 per cent showed improvement. Only 33, or 17 per cent of the total, showed no change in their symptoms (Table I). In the failure group, pneumonitis accounted for one-

7. Lhotka, F. M., *Illinois M. J.*, 112:259,1957.
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TABLE 1.

CLINICAL RESULTS IN 189 CASES OF RESPIRATORY TRACT DISORDERS TREATED ORALLY WITH *TRIAMINIC* TABLETS.

Symptom Complex	Number Treated	Complete Symptomatic Relief	Improved	No Change	Reaction
Acute Upper Resp. Infect.	87	59	17	11	5
Postnasal Drip	47		45†	2	1
Chronic Bronchitis	23	5	9†	9	0
Pneumonitis	10	1	1	8	2
Chronic Sinusitis	8		6†	2	0
Allergic Rhinitis	4		4†		0
Bronchiectasis	3		3†		0
Acute Laryngitis	3	2		1	0
Bronchial Asthma	2		2		0
Acute Adenoiditis with Myringitis	1	1			0
Chronic Recurrent Tonsillitis	1	1			0
TOTALS	189 (100%)	69 (37%)	87 (46%)	33 (17%)	8 (4%)

†Relieved of symptoms as long as therapy was continued.

fourth of the total of 33 cases. There were eight mild reactions including only dizziness and gastrointestinal intolerance, but discontinuation of medication was not necessary. Dosage was reduced in the patient experiencing dizziness.

The following case histories are typical of the results obtained with this oral therapy in acute upper respiratory infection, postnasal drip and bronchiectasis:

CASE 1

A boy of 11, weight 67½ pounds, height 58 inches, was seen with complaints of frequent headache, anorexia, nausea, vertigo, palpation, lassitude and nervousness. A chronic low-grade fever, never more than 100° F., had persisted for some time. There was a previous history of frequent acute upper respiratory infection. Physical findings were negative except for erosion around the left naris, a denuded area of the mucosa, and ulceration in the Kiesselbach area, also on the left side. All laboratory studies were negative and a diagnosis of acute maxillary sinusitis was made two weeks later. One *Triaminic* tablet two times daily, and multiple-vitamins were prescribed.

When seen one month later there was no sinus pain and the condition of the nose was markedly improved. The postnasal drip with its early morning coughing had diminished. Both medications were continued. One month later the patient had no postnasal drip on arising and could breathe through the nose more easily. Headache was gone entirely and there was improvement in his general condition. Color had returned slightly and lassitude was diminished. The patient was instructed to continue *Triaminic* therapy. Ten weeks later the patient was seen for a recurrence of the nose symptoms and the dull aching about the eyes. It was found he had discontinued the medication during the summer. Examination revealed a recurrence of acute maxillary sinusitis and *Triaminic* was prescribed, one tablet at bedtime.

CASE 2

A man of 39 was seen with a complaint of chronic raw throat, which was found to result from a chronic postnasal drip. An antibiotic was prescribed, but after three weeks the patient reported no improvement. At this time 2 cc. of gamma globulin was given intramuscularly. Three days later the injection was repeated. On examination two weeks later there was still some throat soreness and the uvula appeared slightly edematous. Antibiotic packs were inserted, 10 per cent guaiacol in glycerin was painted on the throat, and a long-acting antihistamine was prescribed. After two days he had a severe cough and his throat was still sore. The prescription given him on his previous visit was repeated, and he was instructed to use a hydrocortisone nasal spray four times daily.

A year later cautery was used on a tonsil bag. After three months the patient again returned complaining of a chronic sore throat. One *Triaminic* tablet, twice daily, was prescribed. Ten months later the patient reported that results on this therapy were satisfactory.

Case 3

A man of 45 was seen with a severe cough of many years' duration. Examination revealed a bronchiectasis (greatest in the left lung base) which was confirmed by x-ray, and a severe postnasal drip. During the next two years, various medications including antibiotics, antihistaminics and steroids administered orally or parenterally failed to control the cough. *Triaminic* therapy was instituted, one tablet daily at bedtime. After the first day there was only a slight cough on arising, and sputum had become thinner and less purulent. After 30 days the patient stopped treatment because he "didn't want to get into the habit." The next day his cough was worse and within a week it was as bad as before therapy was started. Treatment was reinstituted with a repetition of the improvement. When last seen, the cough was still satisfactorily controlled.

DISCUSSION

Excellent results have been obtained with oral therapy in a varied group of respiratory tract disorders. Experience indicates that more frequent dosage is desirable in acute cases, while one tablet at bedtime is usually adequate in chronic postnasal drip. In most cases of acute upper respiratory infections, the dosage was one tablet every four hours during waking hours and one tablet at night if the patient was awakened by his symptoms. On a dosage of one tablet every four hours, it was found that some cases which failed to respond to smaller doses in a previous infection responded well in subsequent acute attacks.

In almost all cases with upper respiratory infections treated with this medication, nasal discharge did not progress to the purulent discharge stage. This might be explained on the basis that the medication successfully controlled excessive dilation of the capillaries which may result from the local formation of histamine or "H" substance. The latter vasodilation is said to increase the permeability of the capillaries, with subsequent exudation of protein-rich fluid, an ideal medium for the growth of secondary invaders.[13]

In all but two of the 47 cases of chronic postnasal drip, treatment was successful with one or two tablets daily. The usual dose was one tablet at bedtime, but in a few cases one tablet in the morning and another in the evening were required to provide satisfactory results. In no case was a larger dosage necessary. The efficacy of this medication may be explained by the fact that in many instances, anatomical areas which are important in the management of nasal symptoms cannot be reached by topical medication.[14] Systemic distribution insures adequate concentration of medication over the entire respiratory tract.

SUMMARY

In a series of 189 patients treated for a variety of respiratory tract disorders, symptoms were eliminated in 37 per cent, improvement was noted in 46 per cent and 17 per cent obtained no benefit. There were only eight side reactions, none sufficiently severe as to cause withdrawal of the medication. Oral therapy has been found to be effective in controlling the symptoms of upper respiratory infections, and in other respiratory tract involvements including several that were unresponsive to topical vasoconstrictors. Postnasal drip which had previously been difficult to treat improved in all but two of 47 patients.◀

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ORIGINAL ARTICLE

The Meaning of Eye Symptoms

Some suggestions which may be helpful in the diagnosis, determination of cause, and treatment of many common eye symptoms

WILLIAM H. HAVENER, M.D., *Columbus, Ohio*

The necessity for thorough physical examinations is impressed upon us in medical training, but the demands of practice usually render complete examination impossible. Fortunately, we are directed to the most essential areas for study by the patient's symptoms. Knowledge of the causes of common symptoms is important, for we recognize known and expected entities far more easily than strange ones—particularly when examining the less familiar areas.

Suggestions which it is hoped will prove helpful will be made concerning some common eye symptoms.

FOREIGN BODY SENSATION

In examining a patient with this symptom one may fail to find a foreign body. The particles are usually minute and not easily detected against the transparent corneal background. Severely painful foreign bodies are always imbedded in the cornea or the back surface of the upper lid.

To detect a small corneal foreign body, a bright moveable light such as a small flashlight is essential. Details will be seen much better with illumination directed from the side than from straight ahead. Slow movement of the light will often demonstrate reflections from corneal irregularities or cast characteristic shadows upon the iris, thereby localizing the damaged area. Should pain and the accompanying blepharospasm in-

terfere with examination, a drop of anesthetic such as 0.5% *Ophthaine* will be helpful.

If no corneal foreign body is visible, the upper lid should be everted and the back surface examined carefully. The patient looks down, the lashes are grasped between the thumb and forefinger and pulled forward and *down*, not up. Eversion is accomplished by pushing down with a stick on the upper border of the tarsal plate, at least one centimeter above the lid margin. Once everted, the lid margin is apposed to the brow and held there by the thumb for careful inspection. The appearance of multiple vertical corneal abrasions is pathognomonic of a foreign body behind the upper lid.

If, with the history of eye trauma, no foreign body can be found to account for the painful sensation, the next possibility is a corneal epithelial abrasion. Oblique moving illumination will usually detect this in the mirror-smooth corneal surface. This failing, staining with 0.5% fluorescein solution will color all epithelial defects a bright green. Excess fluorescein is irrigated out with saline.

Corneal ulcers may also produce a foreign body sensation, and are demonstrated by the same methods described for an abrasion. Ulcers will ordinarily be surrounded by a grayish infiltrate. During the early stages of acute conjunctivitis some patients describe a mild foreign body sensation. Irritation from a misdirected eyelash is common. If no other cause for foreign body sensation is evident, the lid margins should be closely inspected for such inturned hairs. Loose lashes may enter the lacrimal punctum or Meibomian gland orifices, from which position they abrade the cornea.

Several common asymptomatic lesions are frequently mistaken for the source of irritation:

1. Lymphatic cysts are transparent or bluish, smoothly rounded structures usually in the inferior cul de sac.

2. Conjunctival concretions are gray or yellow discrete deposits found in folds of the conjunctiva.

3. Pigmented scleral foramina are vessel and nerve exits most prominent in the upper sclera about 5 mm. from the cornea. They are often densely black and may closely simulate a foreign body.

"FLOATERS" IN THE FIELD OF VISION

Opacities which move in relation to the eye represent shadows cast upon the retina by vitreous debris. Although the majority of "floaters" are either benign or untreatable, they may indicate several serious diseases which can be greatly helped by early care. Any patient complaining of a sudden onset of floaters must be given a careful ophthalmoscopic examination through a *well dilated pupil*.

Developmental Remnants

The hyaloid artery and its branches traverse the developing vitreous during intra-uterine life, then atrophy and incompletely disappear. When looking against a light background, almost everyone can see fine linear and punctate shadows. Such opacities are nonprogressive, though they sometimes cause alarm when first discovered. Accidental discovery of hyaloid remnants is by far the most common cause of complaint of "floaters." Nevertheless, the serious nature of many of the other causes indicates performance of an adequate eye examination for such complaints.

why California table wine in the low-sodium diet?

TABLE I[1]

	No. specimens examined	Sodium (mg./100 cc.) Mean
Musts (crushed white grapes)	9	1.63
California Red Table Wines	82	5.56
California White Table Wines	73	5.44
California Dessert Wines	104	7.10

*D*ietary restriction of sodium has become a standard procedure in the control of edema associated with cirrhosis of the liver, congestive heart failure, certain kidney ailments, toxemias of pregnancy, during digitalization and in drug-induced diuresis.

Unfortunately sodium-restricted diets tend to be flat, tasteless, monotonous, leading toward failure of dietary cooperation by the patient.

In such cases California table wine may be employed safely as well as to advantage in making the food more palatable without adding significant amounts of sodium.

In a recent study[1] it was shown that California table wines are remarkably low in sodium content—less than 10 mg. per 100 cc. (3½ ounce glass).

Since recent research [2,3,4] has also shown that wine stimulates a lagging appetite and aids digestion while adding a sparkle to any meal—why not encourage the moderate use of wine by the patient on a restricted dietary, as well as by the sufferer from anorexia, the post-surgical, convalescent or geriatric patient?

May we send you a copy of "Uses of Wine in Medical Practice"? A copy is available to you, at no expense, by writing to: Wine Advisory Board, 717 Market Street, San Francisco 3, California.

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Hemorrhage

Vitreous hemorrhage causes a multitude of large and small floaters, the extent of which varies with severity of the hemorrhage. Often a reddish discoloration of vision is reported. The cause is obvious if there is a history, or evidence, of recent trauma. Traumatic intraocular hemorrhage ordinarily requires ophthalmologic consultation for evaluation of extent of injury and for proper care. Spontaneous intraocular hemorrhage is frequently due to systemic disorders such as diabetes, hypertension, blood dyscrasia, or increased intracranial pressure. Even if the vitreous hemorrhage completely obscures the retina, diagnosis can be made by examining the more normal eye. Examination of the other eye is one of the most valuable aids to eye diagnosis.

Purely ocular disease may cause spontaneous vitreous hemorrhage. Examples include occlusion of the retinal veins, neoplasm, retinal detachment, and inflammation.

Inflammations

Inflammation of the retina or uveal tract is usually of unknown etiology, although viruses, granuloma-producing organisms, and allergy are frequently incriminated. The symptoms of uveitis vary greatly depending upon its location. Quite commonly inflammatory cells gain access to the vitreous and cause the complaint of "floaters." Condensation of inflammatory debris upon the vitreous framework often forms net-like masses of opacities which are disturbing to the patient. Inasmuch as intensive steroid therapy is often valuable in preventing loss of vision, prompt recognition of uveitis is important.

Degenerative Changes

These occur in genetically predisposed eyes or following trauma and inflammation. The most important degenerative disease causing "floaters" is retinal detachment. At the time of formation of the retinal tear, a shower of pigment or red cells suddenly appear in the vitreous. A variable time later, progressive loss of a portion of the visual field is noted. Nearsighted or previously injured eyes are particularly prone to develop retinal detachments. Proper surgery for detached retinas gives good results if done early. Recognition of this cause of "floaters" indicates emergency care.

Vitreous detachment is a relatively common occurrence in older persons. When the posterior surface of the vitreous separates from the retina, small opacities often cling to the vitreous and cast visible floating shadows. Following thorough examination, assurance can ordinarily be given that this condition is usually benign and will not lead to blindness.

SPOTS FIXED IN RELATION TO THE DIRECTION OF GAZE

These are readily differentiated by history from vitreous "floaters." They are due to lesions of the retina or visual pathways. Common causes include senile macular degeneration, chorioretinitis, injury, and vascular occlusion. If ophthalmoscopic examination does not completely explain the defect, visual fields must be done and may permit diagnosis of central nervous system disease. Often the patient does not realize or describe the extent and nature of visual field defects, and simply states his vision is "blurred."

GRADUAL REDUCTION OF VISION IN OLD AGE

This change is fairly common and often is accepted uncomplainingly as a natural accompaniment of advanc-

ing age. It should be emphasized that a healthy eye sees clearly even in extreme old age, and that decreased vision indicates disease—often of a type responding to treatment.

All elderly persons suffer from presbyopia and require proper glasses.

Cataract is one of the most common diseases causing typical, gradual, painless visual loss, which may require years to reach a stage which handicaps the patient. Operation is indicated only for advanced cataract, at such time when the patient no longer has adequate vision. Often an elderly patient is erroneously advised not to see an ophthalmologist until his vision is gone. It is obvious that this advice leads to tragedy should he have glaucoma rather than (or in addition to) cataract.

Glaucomatous visual loss is usually insidious, painless, and not readily differentiated by history from cataract. Glaucomatous loss of vision is, however, *irreversible* and, most important, *preventable* by proper early treatment. Twelve per cent of all blindness is due to glaucoma. Very rarely does the patient recognize his difficulty until a far advanced stage of the disease is reached. It is the duty of the physician to diagnose glaucoma before these late stages are reached.

Senile macular degeneration causes a bilateral loss of central vision, of gradual onset. Patients often realize they have such a central defect, particularly if asked to describe their trouble. Although no treatment is available, comfort is usually derived from knowledge that peripheral vision is never affected by this degeneration. Diabetes or hypertension may cause gradual or sudden visual loss. The cause of diabetic retinopathy is affected very little by medical treatment. There are many instances of dramatic improvement of hypertensive retinopathy through proper systemic treatment. Optic atrophy is another cause of gradual visual loss which may mimic the history of cataract. Treatment depends upon the cause, and may be dramatically effective as in the case of early neurosyphilis or early brain tumor. The average older person believes that all painless and gradual visual loss indicates a need for change of glasses. Commonly he really does need new glasses and also has early serious eye disease. Prescription of glasses without further investigation may permit insidious irreversible visual loss. For this reason the older patient should avoid a non-medical refractionist, and should seek the care of an M.D.

SYMPTOMS OF REFRACTIVE ERROR AND/OR MUSCLE IMBALANCE

These symptoms include almost anything which is clearly related to use of the eyes. A refraction is indicated when use of eyes results in headache, whether occipital, vertex, temporal, frontal, orbital, sharp or dull. Rapid fatigue of the eyes when reading may be caused by refractive error. Blurring of vision, constant or intermittent, often signifies a need for glasses. The physician recognizes that these symptoms may also be caused by intracranial neoplasm or inflammation, ocular disease, mental disorder, or various systemic illnesses. Since the symptoms of refractive error are indistinguishable from those of disease, the only excuse for non-medical eye refractions is the statistical one that myopia and astigmatism are a great deal more common than retrobulbar neuritis or chorioretinitis, and therefore, that the majority of patients do not have a serious disease to be overlooked.

DIPLOPIA

Many people experience diplopia voluntarily through relaxation of their fusion ability. Diplopia of sudden onset often signifies weakness or paralysis of one of the extraocular muscles. This is particularly true if diplopia is more marked in one direction of gaze (in the field of action of the paretic muscle.) Vertical displacement of the double images is almost invariably due to muscle weakness. Diplopia indicates careful examination for the cause, which may be central nervous system disease, orbital pathology, myasthenia gravis, etc.

BURNING AND IRRITATION

These common ocular complaints are often resistant to therapy. Chronic infection of the lid margin is a frequent cause. Excessive exposure to smoke and dust may be responsible. Although allergy may cause these symptoms, itching is its most characteristic manifestation. Tear deficiency is seen particularly in middle aged, arthritic women, or in eyes which have suffered severe conjunctival inflammation, and is often helped by the use of 1% methylcellulose or other artificial tear preparations.

OTHER SYMPTOMS

Watering of the eye (epiphora) is usually due to excessive secretion. The irritation of a foreign body or of ocular inflammation or allergy causes excessive tearing. Inadequacy of the lacrimal outflow apparatus, a less common cause, may occur through ectropion of the lower lid with consequent malposition of the punctum, injury of punctum or canaliculi, or blockage of the nasolacrimal duct.

Photophobia is a nonspecific symptom accompanying many types of ocular irritation and inflammation. Many normal eyes have unexplained hypersensitivity to light.◀

ORIGINAL ARTICLE

Preliminary Report on the Clinical Use of A New Laxative

This new contact laxative produced good results in twenty patients with chronic constipation

JACK SOKOLOW, M.D.,* *New York, New York*

Extensive pharmacologic and clinical studies conducted in Europe during the past five years indicate that bisacodyl†, a new compound with outstanding laxative properties, may be useful in a variety of clinical situations. The compound is practically insoluble in water or alkaline solution, and is not absorbed in significant amounts from the gastrointestinal tract.[1]

A "CONTACT" LAXATIVE

Bisacodyl has been described as a contact laxative. On contact with colonic mucosa after either oral or rectal administration, it promotes evacuation of normally formed, soft stools by inducing peristaltic movements throughout the colon.[2-4] When administered rectally, it may obviate the need for an enema, since it is usually effective within 15 to 60 minutes.[4,5]

Local anesthesia of the colon abolishes the laxative effect of bisacodyl,[6] indicating that it acts by direct stimu-

*Director, Department of Physical Medicine and Rehabilitation, Elmhurst General Hospital, Queens.
†*Dulcolax*® tablets and suppositories, Geigy Pharmaceuticals, Ardsley, New York.

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lation of nerve endings of the colonic mucosa. Studies on isolated segments of colon in experimental animals[1] and on patients with suitable fistulas or colostomies[2] suggest that it initiates peristaltic activity through two distinct nervous pathways: local axon reflexes mediated through the myenteric plexuses, and segmental reflexes mediated through afferent nerves reaching the central nervous system by way of the paravertebral ganglia.

Since the compound is poorly absorbed its toxicity is low, with a therapeutic ratio in animals of 1:200.[1] Because it is quickly eliminated through its own activity, any undesirable effects must be self-limited. Its action is restricted to the colon and does not affect other segments of the gastrointestinal tract,[1] so that cramps and griping are seldom observed.

EXPERIENCE WITH BISACODYL

Bisacodyl was employed for periods up to one month in 20 patients, most of whom were bedridden, and suffering from various disorders. Difficulty of bowel evacuation was common to all of them, and in many cases antedated their period of hospitalization. Numerous remedies had been prescribed before bisacodyl was made available for clinical trial.

This preliminary report concerns observations on two patients treated with bisacodyl and is presented as representative of the results obtained in the entire group. A detailed report of the results in all the patients treated will be published at a later date.

Case 1

A woman of 58 with multiple sclerosis was admitted suffering from chronic constipation of many years duration, for which she used laxatives. Her condition had been complicated by paraparesis and by the presence of an ischiorectal abscess which, despite incision and drainage and subsequent therapy, left a fecal fistula. During hospitalization she was often constipated, requiring enemas and digital extraction. Magnesium hydroxide, cascara extract and mineral oil were also used, with inconsistent results.

At the beginning of this study, she was given a rectal suppository containing 10 mg. of bisacodyl at 6 A.M. that produced a gross watery movement five hours later. On succeeding days, the dosage was reduced to one-half a suppository (5 mg.). This dosage consistently produced an adequate movement of soft, formed stools within one to four hours after insertion. After two weeks, bisacodyl was withheld for one or two days at a time, and in no case did a bowel movement occur until 5 mg. was again administered as a suppository. After the third week, movements occurred regularly approximately one-half hour after the suppository was given.

The patient has been maintained for more than one month on suppositories with satisfactory and regular evacuation. No other laxative measures have been required. There has been no distention, pain, griping, or tenesmus at any time. The use of suppositories continues, for movements occur only after administration of the drug.

Case 2

A man of 54 whose right foot had been amputated within the past year because of diabetic gangrene gave a history of constipation since adolescence, and during the hospital stay after amputation he was continually constipated. Before the start of this study he was receiving magnesium hydroxide and cascara extract several times weekly. This treatment usually produced adequate liquid stools.

A dose of 10 mg. of bisacodyl was administered orally to this patient for the first time in the evening of a day when he had had no bowel movement. This resulted in a moderate movement of hard stools on the following morning. Repetition of the same treatment that evening produced a satisfactory evacuation of softer stools in the morning. Daily oral doses of 10 or 15 mg. given in the evening accomplished satisfactory results on two of the next three days, with the passage of soft, formed stools.

After the occurrence of two movements on the same day, it was decided to withhold bisacodyl. The patient evacuated normally for two days but became constipated again. During the following week, evacuation occurred only once, in response to a 10 mg. oral dose of bisacodyl.

less restricted* night-time sedation

in elderly patients, for instance,

nonbarbiturate Doriden provides 4 to 8 hours of sleep without the pre-excitation and later "hangover" often encountered with barbiturates. Doriden is extremely safe. It is especially useful in the many older patients who cannot tolerate barbiturates or who, because of continued use, require such high dosages that respiration may be depressed.

- ***unlike** barbiturates, Doriden is usually not contraindicated where renal and hepatic disorders are present.
- ***unlike** many barbiturates, Doriden rarely causes pre-excitation; onset is smooth, rapid.
- ***unlike** barbiturates traditionally used for sedation, Doriden is metabolized quickly, thus rarely produces "hangover" and "fog."

SUPPLIED: Tablets, 0.5 Gm., 0.25 Gm. and 0.125 Gm.

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It was then decided to administer the drug to the patient by rectal suppository. On the first evening, an adequate movement of fairly soft stools occurred within an hour after insertion of one 10 mg. suppository. During the following week, movements occurred regularly on 5 mg. by rectal administration.

On discontinuing the laxative, normal evacuation continued each morning, and regular passage of soft stools has been maintained spontaneously up to the present time, a period of two weeks. It appears that a short course of treatment with this drug has re-established a normal cycle of bowel evacuation at least temporarily in this patient.

CONCLUSIONS

These cases, together with others currently under study, indicate that bisacodyl may prove of great value when it is desirable to maintain or restore a regular pattern of bowel evacuation without dehydration and without excessive straining at stool. Doses of 5 to 15 mg. of bisacodyl given either orally or as rectal suppositories have consistently evoked normal evacuation of soft, formed stools without undesirable sequelae.◀

Intestinal Obstruction Due to Bishydroxycoumarin Poisoning

The excellent results achieved by long-term therapy with anticoagulants in cases of coronary thrombosis and recurrent thrombophlebitis have been marred by an occasional severe toxic reaction. Hematuria, gastrointestinal bleeding, and hemoptysis are the most commonly encountered complications. Toxic manifestations of *Dicumarol* therapy producing acute abdominal emergencies have been reported. The case reported represents a rare instance of intestinal obstruction caused by overdosage of the drug.

Pearson, S. C. & MacKenzie, R. J., *J.A.M.A.*, 167: 454-456,1958.

ORIGINAL ARTICLE

Postoperative Acute Adrenal Cortical Insufficiency After Steroid Therapy

If the danger is recognized, simple and effective means may be employed to protect the patient in a state of stress incident to an injury or an operation

WILLIAM D. SEYBOLD, M.D., and
EDWARD A. FITCH, M.D., *Houston, Texas*

The patient who has been receiving ACTH or cortisone may develop acute adrenal cortical insufficiency during operation or the immediate postoperative course. In view of the widespread use of corticosteroids in clinical medicine, it is imperative that both clinicians and surgeons understand some of the consequences of the use of these agents.

Within the past four years at least five fatal cases of acute adrenal insufficiency, which developed during the immediate postoperative period, have been recorded in patients who had received adrenal hormones prior to surgery. One patient was a man, 34 years of age, who died in shock three hours following a cup arthroplasty of the hip.[1] He had been taking cortisone for eight months, right up to two days before operation. Another instance was a woman, 20 years of age, who had taken cortisone for rheumatic arthritis for six months before undergoing a corrective knee operation. The cortisone was discontinued the day before surgery. The patient died in a state of semi-stupor and shock 5½ hours following the procedure.[2] Two more fatal cases

1. Fraser, C. G., et al., *J.A.M.A.*, 149:1542,1952.
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have been reported.[3] The first patient had received cortisone for rheumatoid arthritis for one year. The last dose had been taken the day before gastrectomy for benign ulcer. Immediately after the operation, signs of shock appeared and the patient succumbed three hours later. The second patient, a woman with rheumatoid arthritis, 54 years of age, had received cortisone and ACTH in courses for two years. Exclusive of six intra-articular injections of hydrocortisone, the drugs had been discontinued 4½ months prior to a bilateral bunionectomy. The patient withstood the surgery well, but 15 hours postoperatively shock developed and she died within an hour. Adrenal cortical failure postoperatively was reported in two patients, one of whom survived.[4] The other died 14 hours after simple closure of an acute perforated duodenal ulcer. This man, 62 years of age, had been taking large doses of cortisone almost daily for two years for arthritis. His postoperative course was characterized by hypotension, tachycardia and other clinical signs of shock. Necropsy on each of these five patients revealed severe adrenal atrophy.

CASE REPORTS

Two patients developed adrenal insufficiency following operation.[5]

Case 1.

This is the case of a woman, 58 years of age, who had idiopathic thrombocytopenic purpura. In an attempt to control the hypersplenism prior to splenectomy, she was given 200 mg. of hydrocortisone daily for 15 days. The last dose (50 mg.) was administered 14 hours before operation. The splenectomy required two hours. Blood loss was not excessive and her condition remained stable throughout the procedure. Soon after return to her room, her blood pressure dropped to 100/90, and her pulse rate rose to 128 per minute. One hour later, the blood pressure was recorded as 70/0. Neither examination of the abdomen nor aspiration of the peritoneal cavity yielded evidence of intraperitoneal hemorrhage. An intravenous infusion of norepinephrine in saline was promptly followed by a rise in blood pressure to almost normal levels. Upon slowing of the fusion, however, the blood pressure immediately fell. Since it seemed probable that the shock was due to adrenal cortical insufficiency, 11 hours after operation the patient was given 100 mg. of cortisone intramuscularly in each of three sites, as well as 50 cc. of aqueous adrenal cortical extract intravenously. The quality of the pulse rapidly improved and the rate of the norepinephrine administration was reduced. During the next 12 hours the patient received 1300 cc. of blood, in addition to a continuous intravenous of norepinephrine and 100 mg. of cortisone intramuscularly. A temporary interruption of the norepinephrine 18 hours postoperatively was followed by another fall of the blood pressure to shock level. An additional 200 mg. of cortisone was given. At the end of 24 hours postoperatively, and 13 hours after the initial 300 mg. of cortisone, her blood pressure remained normal upon discontinuance of the norepinephrine. During the next four days, 100 mg. of cortisone was administered intramuscularly every eight hours, and 50 mg. of ACTH was given daily in the vein. Thereafter, the dose of cortisone was reduced daily, being discontinued on the twelfth postoperative day, and her convalescence progressed satisfactorily.

Case 2.

A woman, 66 years of age, who had a radical mastectomy for carcinoma, for two years previously had received daily oral doses of 75 mg. of cortisone for arthritis. The last dose was taken 24 hours before the operation. During the procedure, which lasted four hours, she was given 1500 cc. of blood, and her blood pressure and pulse rate remained within the normal range.

The patient had not regained consciousness after eight hours. Her blood pressure and pulse rate, fairly constant to this time, changed abruptly. The blood pressure fell to 70/50 and the pulse rate rose to 134 per minute. There was no evidence of hemorrhage and her electrocardiogram was normal. An intravenous infusion of norepinephrine solution was begun, and 75 mg. of cortisone was given intramuscularly. The blood pressure rose and she regained consciousness within a short time,

3. Salassa, R. M., et al., *J.A.M.A.*, 152:1509,1953.
4. Downs, J. W., & Cooper, W. S., *Am. Surgeon*, 21:141,1955.
5. Howland, W. S., et al., *J.A.M.A.*, 160:1271,1956.

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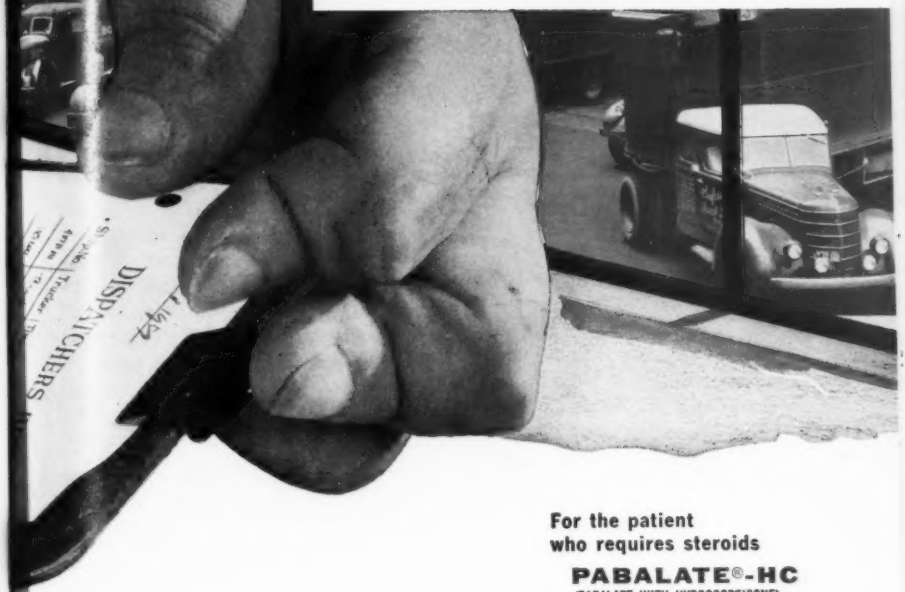

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though when the norepinephrine infusion was discontinued 24 hours after the operation, her blood pressure again fell to 70/40 and she became unresponsive. Another intravenous infusion of norepinephrine was started and 50 mg. of cortisone was given intramuscularly every eight hours.

From this time her recovery seemed assured. Five days later, however, she complained of a headache and on the following day had a generalized convulsion. Subsequent neurologic signs and symptoms led to a diagnosis of cerebral thrombosis. She gradually recovered and was dismissed from the hospital.

DISCUSSION

According to the general adaptation syndrome,[6] the body responds to stress, *e.g.*, surgical trauma or injury, with increased secretory activity of the anterior pituitary. ACTH and other hormones thus elaborated in turn affect the adrenal cortex, producing corticoids. Among the complex actions of the adrenocorticoids is their influence upon the compensatory mechanisms in reversible shock. Although a connection between hypoadrenocortical function and shock has been recognized for many years, the fact that reduced adrenal cortical function may follow the use of ACTH and cortisone is a recent discovery.

In the human subject, partial or complete suppression of adrenal cortical function was first observed subsequent to the removal of a hyperfunctioning adrenal cortical tumor.[7] In 1937 it was demonstrated that the administration of adrenal cortical extract and cortisone to rats resulted in atrophy of the adrenal cortex.[8]

More recently, cinical studies have disclosed abundant evidence of depressed adrenal cortical function after treatment with cortisone. Many patients have complained of weakness and fatigability for varying periods after withdrawal of cortisone. In some patients urinary excretion of 17-ketosteroids is reduced soon after the administration of cortisone, remaining subnormal throughout the therapy and subsequently for an indefinite time. The ability of the adrenal cortex to respond to one or several doses of corticotrophin, as measured by decreased concentration of eosinophils or by increased urinary excretion of corticoids, is diminished by the long-term administration of cortisone. Adrenal cortical atrophy has been found at necropsy in some patients who have received cortisone for no longer than five days. Degenerative changes (so-called Crooke's changes) in the pituitary gland of patients treated with cortisone have been observed, and the same changes have been described after treatment with corticotrophin.[9]

DEDUCTIONS

From the evidence presented, it seems reasonably clear that cortisone is capable of producing atrophy of the adrenal cortex and that this atrophy is accompanied by impairment of adrenal cortical function. Both the atrophy and the functional impairment may persist after withdrawal of the cortisone, perhaps for a long time. Adrenal atrophy and impaired function may lead to acute adrenal cortical insufficiency in the presence of sufficient stress, such as is associated with an operation or injury. These effects are due entirely to suppressed production of endogenous corticotrophin by the pituitary. The last observation suggests that administration of corticotrophin may carry the same risk as that of cortisone.

6. Selye, H., The Physiology and Pathology of Exposure to Stress: A Treatise on the Concepts of the General Adaptation Syndrome and the Diseases of Adaptation, Montreal, ACTA, Inc., 1950.
7. Walters, W., et al., *Ann. Surg.*, 100:670,1934.
8. Ingle, D. J., & Kendall, E. C., *Science*, 86:245, 1937.
9. Ward, L. E., et al., *J.A.M.A.*, 152:119,1953.

A CIBA Documentary Report

How clinicians evaluate the safety and effectiveness of RITALIN® as a psychic stimulant

CONDITIONS TREATED	RESULTS	COMMENTS ON SAFETY
Depression accompanying chronic illness and convalescence from short-term illness; mild depression induced by life pressures; overtranquilization.	"The drug gave a plateau type of stimulation, smooth onset, with no euphoria . . . The effect lasted about four hours, gave the patient a feeling of well-being . . ."	"The side effects of Ritalin are minimal." "The work showed that the drug had no effect on blood pressure, the blood count, urine or blood sugar, did not depress the appetite, and produced no tachycardia."[1]
Lethargy, fatigue and emotional depression secondary to chronic illness in elderly patients; mild depression secondary to short-term illness. (Twenty-three "normal," healthy people also received the drug.)	"For the entire 112 patients 66 per cent showed marked improvements [obvious drug effect and mood improvement] . . ."	"No serious side reactions were noted . . . In no case was it necessary to stop the drug. No evidence of significant effect upon blood pressure or pulse has been found. This is particularly interesting, since these side effects have been common with other mood elevating drugs . . ."[2]
Drug-induced psychophysiologic depression; physiologic after-effects of certain anesthetics; barbiturate intoxication; moribund states due to systemic infection. (All patients were epileptic, mentally retarded and/or brain damaged.)	"All except two [of 129] patients responded to the initial injection [of parenteral Ritalin] within 1½ to 15 minutes."	"In no instance was there any evidence of untoward effects." ". . . the very poor basic physical condition of our patients in this study, those associated with profound chronic brain damage, accentuates the safety of parenteral Ritalin . . ."[3]

DOSAGE: *Oral:* Dosage will depend upon indication and individual response. Many patients respond to 10 mg. b.i.d. or t.i.d. Others will require 20-mg. doses. In a few cases, 5-mg. doses will be adequate. If inability to sleep is encountered, last dose should be given before 6 p.m. *Parenteral:* 10 to 30 mg., intravenously or intramuscularly.

RITALIN® hydrochloride (methylphenidate hydrochloride CIBA)

2/2593HK

References: 1. Natenshon, A. L.: Dis. Nerv. System 17:392 (Dec.) 1956. 2. Landman, M. E., Preisig, R., and Perlman, M.: J. M. Soc. New Jersey 55:55 (Feb.) 1958. 3. Carter, C. H., and Maley, M. C.: Dis. Nerv. System 18:146 (April) 1957.

CIBA SUMMIT, N. J.

MANAGEMENT

The management of the surgical patient who has received ACTH or cortisone comprises three phases.

1. The recognition of the likelihood of acute adrenal insufficiency following an operation.

2. The institution of measures to preclude this complication.

3. The treatment of acute adrenal cortical insufficiency when it appears.

Postoperative adrenal cortical insufficiency incident to previous therapy with adrenal or pituitary hormones is uncommon, but it has been reported fatal to several patients, and it is not possible to determine prior to operation those who are susceptible and those who are not. It seems proper to assume that any patient who has received cortisone in significant quantities within three to six months before surgery should be given prophylactic therapy. The evidence suggests that patients with clinical hypercortisonism, either natural or induced, may be more subject to acute adrenal insufficiency than those who have had mere maintenance therapy. It has been recommended that such patients be given prophylactic therapy if operation is undertaken within 12 or 18 months after hormones have been discontinued.[3]

PURPOSE OF PREOPERATIVE THERAPY

This provides a depot of sufficient adrenal steroid in the muscle to insure an adequate and continuing supply of adrenal hormones at critical times during and after operation. The following regimen has been proposed by Salassa et al.: 200 mg. of cortisone at 48 hours, 24 hours, and one to two hours before operation. The dose is gradually reduced after operation, both the rate of reduction and the duration of therapy depending upon the condition of the patient. Usually, treatment may be discontinued after three or four days.

PRECAUTIONS

Patients should not be subjected to prolonged fasting. If possible, the operation should be performed in the morning. Patients should not be given excessive quantities of glucose in distilled water.

The postoperative management of the water and electrolyte balance in patients with real or potential adrenal insufficiency is at best a difficult matter. Such patients poorly tolerate abundant quantities of water. They appear oversensitive to narcotics. Morphine and related substances should be administered in small quantities and with caution.

RECOGNITION

The diagnosis of acute adrenal cortical insufficiency following operation or accidental trauma depends upon a familiarity with its manifestations. It is most likely to appear during the first 24 hours after operation or injury. The initial signs are usually a fall in blood pressure, rise in pulse rate, and perhaps fever. The patient may become unconscious rather quickly or, fail to regain consciousness after anesthesia. Any of these signs demand vigorous emergency treatment; normal saline solution with norepinephine should be administered intravenously at once. Intravenous hydrocortisone should be given promptly—the recommended dose is 100 mg. in 500 or 1000 cc. of normal saline over a period of two to ten hours, and repeated. In an acute emergency, 50 mg. may be given the first hour, then reduced to 10 mg. per hour. Cortisone 200 mg. should

be given intramuscularly, to become effective after the first 24 hours. Cortisone given orally is suitable for the patient who is conscious and not nauseated. The duration of the effect is probably less than eight hours, however and under the circumstances its use should be confined to the period of "tapering off" after the condition of the patient has been stablized.

SUMMARY AND CONCLUSIONS

1. ACTH and cortisone are capable of producing atrophy of the adrenal cortex.

2. This atrophy may be associated with impaired adrenocortical function

3. Both atrophy and functional impairment may persist after withdrawal of ACTH or cortisone.

4. These changes may lead to acute adrenal cortical insufficiency during the stress incident to an operation or serious injury.

5. Acute adrenal cortical insufficiency may be prevented if a depot of adrenal steroid in the muscle is provided to insure an adequate and continuing supply of adrenal hormone at critical times after injury or during and after operation.

6. The recognition of acute adrenal cortical insufficiency depends upon one's alertness to the possibility of its development, and familiarity with its signs.

7. Its development constitutes an emergency which requires prompt treatment with intravenous hydrocortisone and intramuscular cortisone or hydrocortisone.

8. Since prompt treatment is not always successful, preventive measures offer the safest and easiest course.

9. Every patient who is to have an operation should be questioned with respect to previous treatment with cortisone or ACTH. Any patient who has received these hormones in significant amounts within three to six months should be given prophylactic therapy.

10. The possibility of acute adrenal insufficiency secondary to ACTH or cortisone medication should be considered in the severely injured patient in shock who does not respond to the usual restorative measures.◀

Pruritus from Bird Mites

A woman of 35 had nocturnal itching of the face, arms and legs for eight weeks with a crawling and stinging sensation of her skin. Other members of the household were not affected. She was seen by internists and dermatologists who, after studies of blood sugar, complete blood cell counts, urinalyses, serologic tests for syphilis, and liver function studies, concluded that her symptoms were "psychosomatic."

When first seen, she had already taken numerous tranquilizers. A crawling object on her skin was found. Treatment consisted of thoroughly cleaning and air-conditioning the room, and using general hygienic measures.

Animal mites may be the vectors of serious systemic disease. While bird mites are an unusual cause of pruritus, they should be considered in the differential diagnosis, especially when the patient does not respond to routine therapy.

Cahn, M. M., & Shechter, F. R., *J.A.M.A.*, 167:724-726,1958.

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References

1. Arner, O., and Others: Nord. med. *58*:1346 (Sept. 12) 1957.
2. Wilner, S.: Canad. M. A. J. *77*:199 (Aug. 1) 1957.
3. Bruner, J. M. R.: U. S. Armed Forces M. J. *6*:469 (April) 1955.
4. Diamant, A. H.: Nord. med. *48*:1324 (Sept. 26) 1952.
5. Wendt, G. R., and Cameron, J. S.: Personal communication, Jan. 4, 1955.
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for the man who "can't go on" after 4:30

Many of your patients probably suffer from brief spells of dejection. Frequently these "letdowns" appear at the same time each day: at 4:30 in the afternoon to the man in his office and at 8:30 in the morning to his wife, after she's seen her husband and children off to work and school.

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ORIGINAL ARTICLE

Treatment of Acne With A New Cleansing Agent Inducing Patient Cooperation

This cleansing agent with additive bacteriostatic action was beneficial to 206 patients with acne vulgaris

JANITH STEWART KICE, M.D., *Garden City, New York*

As the causes of acne vulgaris are manifold, so are the forms of therapy, and the continuing search for promising therapeutic agents which will add to the physician's armamentarium is endless. All agree that scrupulous cleansing is essential, to remove dust, dirt, bacteria, follicular plugs, and excessive oiliness. Repeated use of soap removes the skin's natural acid protective coating, thus lowering its resistance to bacterial invasion. In the past few years soap substitutes and detergents have become popular. Of the three commonly used types of detergents, the anionic is the one under present consideration.

SUCCESSFUL TREATMENT DEPENDS ON REGULARITY

The success of treatment is in direct ratio to the regularity with which a prescribed regimen is carried out. The adolescent or young adult with acne may at first accept therapeutic directions with enthusiasm and a firm resolve to help himself to a better appearance. However, any unpleasantness, difficulty or excessive time required for application of medication may soon lead to the abandonment of the good intentions. This is particularly true when benefits of therapy are not immediately apparent. For this reason, a form of cleans-

ing that is simple and pleasant to use offers the probability of continued use and of greater therapeutic success. A corrective cleansing agent for the acne patient should perform three distinct actions — reduce excessive oiliness, act as a keratolytic, and act as a bacteriostat.

An anionic (alkyl aryl sulfonate) detergent bar containing 8% lanolin and 2% of the degerming agent, bithionol, was found to be effective.[1] This formulation with the antiseptic reduced to 1% and a later modification of this revised formula containing in addition 2% salicylic acid and 2% colloidal sulfur, now known as *pHoam Cleanse Pac*,* was used in this clinical investigation.

TRIAL TREATMENT OF 300 PATIENTS

The two types of formulations offered for the hygienic care of the skin were employed in this study of over 300 patients with a preponderance of acne vulgaris. Each inert polyurethane sponge-like applicator contained one of the two medicated cleansing agents. Usually, the bar containing bithionol, 2% salicylic acid and 2% sulfur was prescribed for maximum drying and healing action. A maximum effect is desirable in the majority of acne cases to eliminate excessive oiliness, to hasten the healing process and to help bleach pigmented scars. In some fair-skinned individuals, it is necessary to switch from the cleansing agent with sulfur and salicylic acid to the one with the bithionol alone, as the former causes too much drying and peeling in a small percentage of patients.

METHOD OF USE

Two of the detergent bars are inserted into the applicator. The applicator is then held under warm water and squeezed vigorously half a dozen times. A foamy lather soon appears on the surface and is applied to the skin of the face, chest and other affected areas with a continuous kneading action. The combination of the medicated foam and the massage enhances the benefits of the washing procedure. Unlike the face brush which is too harsh for sensitive or blemished skin, and the wash cloth which is too soft for a true massaging action, the applicator is stimulatory without being traumatic. This daily massage helps to improve the skin tone and restore the sebaceous apparatus to normal functioning while the keratolytic action of sulfur and salicylic acid separates the dead epithelial cells from the skin and loosens the obstructive comedones.

MODE OF ACTION

Each of the two formulations dissolves in water to form a solution with a pH of 6.9 which falls within the normal (3.7 to 7.0) pH range of the skin and the damage of continued application of alkaline materials to the skin is avoided.[2] While the lubricating effect of superfatted soaps has never been established, the best penetration of salicylic acid has been obtained in a lanolin base and may account for some of the keratolytic action noted with this agent.[3] No sensitivity to the lanolin has been apparent, even in sensitive individuals. The antiseptic and somewhat fungistatic agent, bithionol, is effective *in vitro* against 21 organisms commonly found on the skin, and is a factor in the ef-

*pHoam Cleanse Pac® supplied by Doak Pharmacal Company, Inc., New York.

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3. Flesch, P., et al., *J. Invest. Dermat.*, 25:289,1955.

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Current Concepts in Therapy: Sedative-Hypnotic Drugs II. Chloral Hydrate. New England J. Med. 255:706 (Oct. 11) 1956.

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TABLE I
A SERIES OF 244 CASES OF ACNE VULGARIS
TREATED WITH pHOAM CLEANSE PAC®

Distribution of Patients

By Age		By Duration Of Acne Lesions		By Response To Treatment		
8 - 15 years,	87	1 year or less,	89	Satisfactory,	206	84.4%
16 - 25 years,	103	1 - 5 years,	95	Unsatisfactory,	9	3.6%
26 - 35 years,	44	5 - 10 years,	33	No Follow-up,	29	12.0%
36 - 48 years,	10	10 - 25 years,	11			
		Indefinite	16			
Total	244	Total	244	Total	244	100.0%

ficacy of this product.[4] It is additive on the skin, inhibiting the growth and reproduction of susceptible skin bacteria even at the extremely low concentration of 10 parts per million. It is absorbed and adsorbed by skin and hair, resisting removal by soap and water, and maintains a lowered bacterial count for a long period after application. Using the method of Cade, the average bacterial reduction was nearly 92% with a 1% concentration.[5] Bithionol U.S.P. is not inactivated by proteins and fats of the skin, organic vehicles of soap, or most components of toilet preparations.

PARTICULARS OF THE STUDY

Acne vulgaris had been present in 244 patients, from 4 to 48 years of age, for periods of from less than one year to as long as 20 years. (Table 1). All patients in the group were placed on the same dietary, lotion and physio-therapy regime. The applicator and its cleansing agent was the only variant in the study. Instructions to the patients were individualized according to the skin type and the presenting problem. The bithionol-salicylic acid-sulfur detergent bar was employed with greater frequency. Patients who felt a sensation of "tautness" after washing were directed to rinse their skin immediately. The patients with oily skin are directed to allow the film to remain on the affected areas for 5 to 10 minutes, or even longer, before rinsing.

Comedo formation is aided by the absence of an effective hair penetrating the mouth of the follicle, hence, as the comedones are eliminated, there is more normal hair growth and less subsequent comedo formation.[6]

IN SEBORRHEIC DERMATITIS

Seborrheic dermatitis, with acne vulgaris or alone, may cause an erythematous scaling of the face, center of upper chest and back. The "Pac" not only cleans, but medicates the skin with the acne-seborrheic diathesis and leaves a bacteriostatic agent on the skin for several hours. This eliminates several washings as some cleansing agents are used as many as six times a day in severe cases of pustulation. This method of skin cleansing appears to be more convenient than other methods, which may be a factor in its therapeutic value.

RESULTS

Of the total group of 244 patients, 206 or 84.4% showed a satisfactory re-

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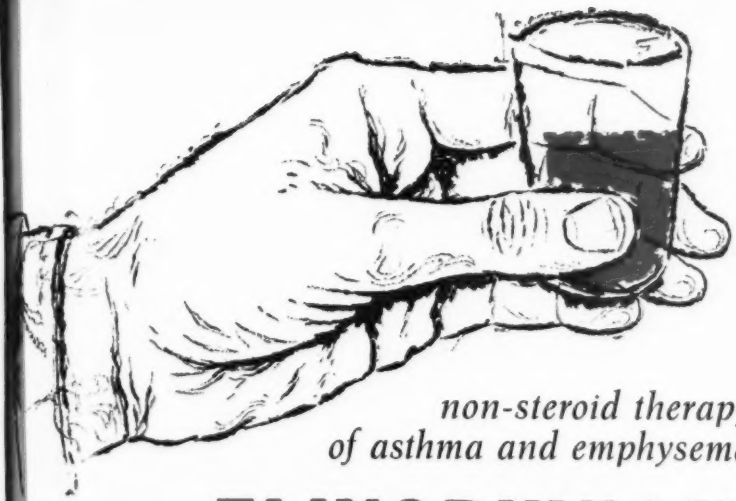

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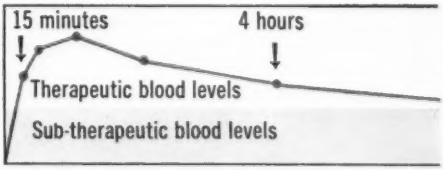
This predictability of blood levels permits quite constant *therapeutic blood levels night and day,* providing relief of wheezing, dyspnea, cough, and protection against acute attacks for most patients.*

DOSAGE: *First two days:*
45 cc. *(three tbsp.)* on arising;
45 cc. *(three tbsp.)* on retiring;
45 cc. *(three tbsp.)* once midway between above doses *(about 3 P.M.)*



After two days of therapy the size of doses should be slightly decreased.
Each tablespoonful contains: theophylline 80 mg., alcohol 3 cc.
Prescription only – bottles of 16 fl. oz.

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sponse. Only 9 patients (3.6%) were not benefited. No follow-up was possible in 29 cases. In most instances improvement in skin tone and appearance was noticeable after one week of use. Both the agent and the method of application were well tolerated. No evidence of primary irritation or sensitization was noted. Only one patient with seborrheic dermatitis exhibited an exacerbation of the condition. The wide patient acceptance of the applicator and the convenience of this method of washing makes possible more assured adherence to prescribed schedules.

CONCLUSION

An improved therapeutic response in 206 cases of acne vulgaris is attributed to patient acceptance and usage of this cleansing technique. The sponge-like applicator facilitates the application and penetration of degerming and keratolytic agents and has encouraged patient cooperation in carrying out a prescribed regimen. A more rapid improvement in skin tone, appearance and healing rate was achieved in 84.4% of the patients. Other patients with varied dermatoses included in this series of more than 300 patients also significantly benefited.◀

Drug-Induced Depression: Fact or Fallacy

To determine whether depression is or is not a "side effect" of tranquilizer therapy, 70 patients with a provisional diagnosis of "drug-induced depression" were subjected to a thorough psychiatric survey, including a follow-up of each patient's subsequent course, in some instances for as long as three years.

The patients were aged 40 to 70; most of them were chronically anxious, subject to mood swings for years. Such persons are liable to depression in the involutional period. Many carry on despite their symptoms until they are laid low by a depression in later life.

If it is assumed that the patient was depressed at the time the drug was started; time and the natural course of the depression could account for the symptoms becoming more overt in three months to two years. Considering the large number of patients who have been treated with small to large doses of *Thorazine* and *Serpasil* for as long as three to four years without becoming depressed, it is difficult to conclude that these drugs and other tranquilizers are depressive. There is a need for greater diagnostic accuracy — before treatment with a tranquilizer as an antihypertensive or for psychiatric reasons is instituted.

Ayd, F. J., Jr., *New York J. Med.*, 58:354-356,1958.

ORIGINAL ARTICLE

Dermatological Hazards From Epoxy Resins

The epoxy resins, most curing agents, and some additives used in industrial plants present various dermatological hazards

GEORGE E. MORRIS, M.D.,* *Boston, Massachusetts*

Epoxy resins cause dermatitis, conjunctivitis and rhinitis in workers. Many industrial plants are now handling epoxy resins, and in my experience it has been found that neither the worker nor his employer has been alerted to the dermatological and ophthalmological hazards involved in their processing. An official of the U.S. Public Health Service recently stated that there is hardly a plant he has visited, using these resins, where dermatoses have not been caused thereby.[1]

Epoxy (ethoxylene) resins are now appearing in widely different types of industry. They are being used as surface coatings (including paints), adhesives, molding compounds, for casting and encapsulation purposes, and as laminates and prosthetics; they are being used to reinforce other plastics, and also to make other plastic tools and dies.[2,3]

Epoxy resins are synthetic resins obtained by the condensation of phenol, acetone, and epichlorohydrin.[4] Chemically speaking, they are "polyethers with terminal epoxide groups,"[5]

*Member of the Committee on Occupational Dermatoses of The Council of Industrial Health of the American Medical Association, member of the Committee on Dermatology of the Industrial Medical Association.

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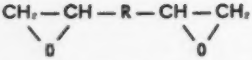

and they are either liquids or solids depending upon the length of their chain "R."

Surprisingly, very little has appeared in the United States medical literature on this currently important subject of dermatoses from epoxy resins. Other than two full-length monographs devoted to this subject[2,6] and one study as to their toxicological hazards,[7] there have been only short references to them in the medical journals of this country. Meanwhile, however the European literature has been far more prolific.[8-14]

EPOXY RESINS AND SOME ADDITIVES AND SOLVENTS ARE OFFENDERS

During their processing stages, particularly when handled by workers in the liquid state, epoxy resins represent severe skin sensitizers and skin irritants, as do the liquid amines which are usually employed as curing agents ("hardeners"). Solvents and reactive diluents are among other chemicals used in processing. Some solvents currently employed for dilution purposes are toluene, xylene, acetone and methylethylketone. Workers use solvents to remove the epoxy compounds from their skin. Such application of solvents directly to the skin represents one of the leading causes of industrial dermatitis. Reactive diluents commonly added to reduce viscosity are styrene oxide, allyl glycidyl ether, phenyl glycidyl ether, and acetonitrile. Both the solvents and the reactive diluents are skin sensitizers and irritants. Workers engaged in processing epoxy resins and mixing in these additives are prone to develop an erythematous eczematous dermatitis on the central third of the face—the nose, the adjacent portions of the cheeks, the upper lip, and the eyelids—as well as on the hands and forearms.[2]

The following cases from my files show variations in the typical picture just described:

Case No. 1

A woman factory worker had an erythematous vesicular eruption of the dorsum of the hands and forearms, but no eruption of the face.

Case No. 2

A telephone worker spliced cables in dugouts. This involved mixing the epoxy resins and the amine hardener together while in the closed area. He developed a dermatitis, and when seen had an acute erythematous eruption of the central third of the face, including the eyelids, the nose and the cheeks. He also complained of irritation of his eye, with redness and watering, sometimes of one eye, and sometimes of both eyes. The eye irritation has since been described by Hine et al[7] and is familiarly known in California chemical plants as "eyeball itch" and described as a "peculiar inflammatory conjunctivitis with rather pronounced granulation of the lower lids."

In addition to prior articles which I have written on the subject of the dermatological hazards involved in handling epoxy resins,[2,15] I have observed and am reporting a case of allergic rhinitis due to the inhalation of chemicals during the processing of epoxy resins:[16]

Case No. 3

A female factory worker had been mixing and pouring epoxy resins for eight

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7. Hine, C. H., et al., *Arch. Indust. H.*, 17:129-144, 1958.
8. Bourne, L. B., *Tr. A. Indust. M. Off.*, 6:94-95, 1956.
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12. Bourne, L. B., (Letter to the Editor relative to Ref. #11 above), *Lancet*, 1:997,1957.
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14. Morgan, J. H., *Brit. J. Clin. Pract.* 11:944-948, 1957.
15. Morris, G. E., *New England J. Med.*, 258:618-619,1958.
16. Morris, G. E., Allergic Rhinitis Acquired During the Processing of Epoxy Resins—to be published.

months. Shortly after commencing employment, she consulted her local practitioner for what she thought was a sinus condition, evidenced mainly by a running of the nose and frequent sneezing during the day (especially while weighing the chemicals in the plant), and by nasal obstruction while in bed at night. Upon being referred to a nose specialist, sinus x-rays were found to be negative, and the diagnosis of rhinitis due to inhalation of fumes at work was made.

This patient was then referred to the author for treatment of a dermatitis of the hands of six months' duration. A diagnosis of contact dermatitis due to handling epoxy resins was made, and in addition to routine treatment, the patient was removed from contact with epoxy resins for a period of one month. Her dermatitis then cleared, the nasal irritation subsided remarkably, and she stated that she could then go to bed at night without feeling that she was going to suffocate.

It was established that on mixing the epoxy resins and the amine hardener, the heat evolved caused fumes to be dispersed into the air and inhaled by nearby workers.

RECOMMENDATIONS

In any plant where processing of or with epoxide resins takes place, the following recommendations should be observed:

1. Management must be seriously interested as to the nature of the materials that their employees are called upon to handle with regard to their chemical content and to the dermatological and toxicological hazards involved.

2. Workers should be given initial and repeated instructions that epoxy resins, and in particular their amine hardeners, and many of the chemicals handled during processing are potent skin sensitizers and irritants. Therefore, they should be impressed with the importance of being extremely careful not to spill these materials, of avoiding any skin contact, and of immediately washing off from their skin any splattered or spilled material. In particular, such workers should be instructed not to use solvents in removing these substances from the skin.

3. Management should provide appropriate working areas, cleaning facilities, and protective clothing. For example, when weighing and mixing these resins, it has been found best to have one worker perform this function in an adequately ventilated area, completely separated from other workers. Workers should be made to take daily showers, baths, and to change from their work clothes to clean clothing on leaving their work. Long gauntlet-type gloves should be worn, with light protective clothing covering the rest of the body. Since most of the hardeners now in use are markedly alkaline, an acid-type cleaner is recommended that will preserve the natural acid character of the skin. Such a cleaner is now being tested for its efficacy in removing epoxy resins, but complete data as to the results are not available at this writing.

4. Persons who have had prior sensitization dermatitis should not be allowed to work with epoxy resins.

It should be observed that the chemical industry at present is engaged in developing low-toxicity hardeners[17] which may serve to reduce the incidence of eruptions from epoxy resins. Some of these are now on the market.

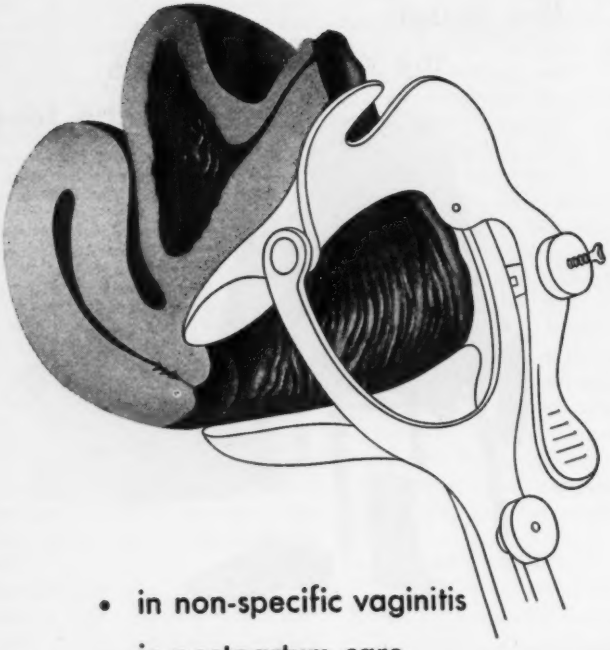
SUMMARY

Epoxy resins cause dermatitis, conjunctivitis and rhinitis.

The epoxy resins, most curing agents, and some of the additives are skin irritants and sensitizers.

Workers and management should be informed as to the hazards involved in processing epoxy resins.◀

17. Low Toxicity Epoxy "Couplers": Hardeners With Lower Skin Irritation Offer Means to Overcome Major Deterrent to Full Development, *Chem. & Eng. News*, 10:4815-4816,1956.



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- in postpartum care
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The "Unexplained" High Erythrocyte Sedimentation Rate

When a high erythrocyte sedimentation rate is found, particularly in older patients, a careful investigation is recommended

BARBARA ANSELL, M.B., M.R.C.P., and
E. G. L. BYWATERS, M.B., F.R.C.P., *London, England*

Routine estimation of the erythrocyte sedimentation rate (E.S.R.) sometimes reveals an inexplicable value in terms of the clinical diagnosis, *e.g.*, when the condition is thought to be non-inflammatory, such as degenerative joint disease. Such cases often remain diagnostic problems.

METHOD AND MATERIAL

Using the Westergren method, 51 of 900 estimations on new patients were found to be above 20 mm. per hour, for no apparent reason. Of these 51 cases, 45 were re-examined and the E.S.R. was estimated again within one month of the first visit. In 14 it had returned to normal, so these patients were classified as having had a transient rise.

Another re-examination of those in the first group was made, with particular search for evidence of tissue destruction or inflammation. No abnormality which could account for the high E.S.R. was found. A chest x-ray examination, a full blood count, and a second urine examination were then done, with negative results.

Since a raised E.S.R. may be the only sign of serious disease such as carcinoma or myelomatosis, further

investigations including electrophoresis of the serum for protein pattern, differential agglutination titer (D.A.T.), C-reactive protein, fibrinogen estimation, L.E. cell search, antistreptolysin titer, and serum uric acid were done. According to the results of these, other investigations were then instituted, including barium meal, barium enema, intravenous pyelography, and electrocardiography. In all cases with joint symptoms a careful review of the x-ray films was undertaken, and in certain cases biopsy of the bone marrow or synovial membrane was made. The patient was hospitalized for these.

RESULTS

In only a small number of cases was it possible to establish the cause of the raised E.S.R. after preliminary investigations, but the follow-up has allowed us to make a diagnosis in 20 of the 31 patients in group I, and in seven of 14 patients in group II. In a large number of patients who were thought at first to have solely degenerative joint disease, a final diagnosis of rheumatoid arthritis was made.

Such final diagnosis was made in patients with polyarthritis with a positive D.A.T., with erosions on x-ray films, or with low viscosity high-protein-containing synovial fluid without infection. The final diagnosis of probable rheumatoid arthritis was made in patients with neither a positive D.A.T. nor x-ray erosion, but in whom pain, swelling and limitation were present in multiple joints over a period of at least six months, without evidence of other conditions.

DISCUSSION

Although the E.S.R. is higher in women (0-20 mm. per hour) and shows some day-to-day variation, apart from menstruation and pregnancy, in normal adults it does not exceed the value of 20 mm. in one hour. As age increases, the sex difference is less obvious and the normal level tends to rise, showing a wider range.

In group I, 15 patients were over 60 years of age, 10 were between 50 and 60, and six under 50 years of age. However, of those in whom an adequate explanation for the rise in E.S.R. was not evident, only three were over 60, five between 50 and 60, and three under 50 years of age. Two cases in the oldest group have remained in good health and were followed for three and two years, respectively. The E.S.R. remained between 20 and 30 mm. in one hour. It is not likely that the raised value is due solely to age and random variation, since in a third similar case the E.S.R. settled under observation in five months.

Of 31 cases in group I, a disease process was diagnosed in 20, although in some it did not become obvious for some time.

The high incidence of rheumatoid arthritis in patients of advanced years and the difficulty in establishing its diagnosis are of particular interest. Clinically, a fairly confident diagnosis was made in 14 of the patients, though only eight fulfilled the criteria described earlier.

SUMMARY

An unexplained rise of the sedimentation rate above 20 mm. in one hour was found in 51 of 900 new patients attending a rheumatology clinic over a period of three and one-half years.

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- acts directly on colonic mucosa[10]
- virtually no contraindications[1-13]
- very well tolerated[1,2,3,9,11-13]

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Suppositories: One at time bowel movement is required.

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acts directly on colonic mucosa
does not depend on systemic absorption

references
(1) Foertsch, A.: Deutsche med. Wchnschr. **78**:916, 1953. (2) Frankl, R.: Medizinische **No. 49**:1587 (Dec. 5) 1953. (3) Krueger, H. H., and Piegsa-Quischotte, I.: Aerztl. Wchnschr. **8**:891 (Sept. 11) 1952. (4) Scheel, M.: Hippokrates **26**:624, 1955. (5) Stockmeier, F.: Muenchen. med. Wchnschr. **95**:1058, 1953. (6) Ganz, P., and Zindler, M.: Medizinische **No. 29/30**:1042, 1955. (7) Kolshorn, R.: Muenchen. med. Wchnschr. **96**:949, 1954. (8) Clark, A. N. G.: Brit. M. J. **2**:866 (Oct. 12) 1957. (9) Aue, H.: Medizinische **No. 3**:118, 1954. (10) Schmidt, L.: Arzneimittel-Forsch. **3**:19, 1953. (11) Barth, H.: Deutsches med. J. **4**:415 (Aug. 15) 1953. (12) Brandt, G., and Brandt, W.: Landarzt **30**:589, 1954. (13) Vieth, H.: Therap. Gegenw. **94**:60, 1955.

GEIGY
ARDSLEY, NEW YORK

Thirty-one of these remained high over one month, and eight of them developed typical rheumatoid arthritis, while six are probably suffering from this disorder. In 11 others no cause for the raised E.S.R. could be found, and their general health has remained good. In five the E.S.R returned to normal within one year, while in six it has remained high.

The finding of a high E.S.R. does not necessarily justify a bad prognosis.◀

Brit. M.J., 1:372-374,1958.

Radioactive Iodine in the Treatment of Angina Pectoris

Because patients having angina pectoris as a result of coronary artery insufficiency usually show progressive improvement with conservative medical treatment, the great majority are not candidates for this type of therapy. Patients bedridden with status anginosus, candidates for radiation, also deserve an adequate period of observation. Such pronounced symptoms represent severe disease and these patients either improve promptly or do not survive. Since the advent of this method of treatment, it has been possible to practically dispense with surgical treatment of this disorder.

Thirteen patients were treated with radioactive iodine. The first received all the radioactive iodine in a single dose, for the others the dose was divided into two parts and given at weekly intervals if the total dose desired was greater than 15 mc. If the 24-hour iodine uptake demonstrated that an adequate dose would be 15 mc. or less, a single dose was given. Using the 24-hour I^{131} uptake to determine the dose administered, the smallest dose was 8.2 mc., the largest 34 mc. These patients were all euthyroid, with intractable angina pectoris despite long periods on standard methods of therapy. One patient who had received a total dose of 30 mc., given in two doses of 15 mc. one week apart developed mild thyroiditis. His I^{131} uptake prior to treatment was 22.8 per cent. This patient experienced no increase in the severity of angina during this period of thyroiditis.

Six of the 13 patients required more than one course to lessen the severity of the angina. At least two months are required for the full effect of I^{131} to become manifest.

Symptoms of myxedema were so severe in three patients as to require thyroid medication. Two patients requiring thyroid to keep them comfortable had poor results as to any change in their angina. The third patient was given small enough doses of thyroid, so that he was not uncomfortable from myxedema and yet was almost free from pain.

Moores, K. D., & King, R. L., *Bull. Mason Clin.*, 12:18-22,1958.

Viral Hepatitis

Convalescence after viral hepatitis may require many months of rest and close followup

JOHN RADCLIFFE EWAN, M.D., *Washington, D.C.*

Viral hepatitis has been differentiated from other diseases causing jaundice only in late years. It is associated with wars and disasters and with the living of human beings in close quarters. Sporadic cases may spring up in uncrowded areas.

Homologous serum jaundice was first described in Bremen, Germany, in 1885. Thousands of cases were produced during World War II in this country by the administration of yellow fever vaccine to Army personnel. In 1955 the United States Public Health Service ranked viral hepatitis fifth among infectious communicable diseases in this country.

ETIOLOGY

Two etiologic types of the disease are recognized: infectious hepatitis caused by virus A (IH virus) and serum hepatitis caused by virus B (SH virus). Infectious hepatitis has an incubation period of two to six weeks; transmission is by ingestion of contaminated food and water or close personal contact with carriers. Serum hepatitis requires an incubation period of 1½ to six months; transmission is by the parenteral route following transfusions or utilization of inadequately sterilized syringes. Dissemination is possible through insect factors and sexual contamination.

PATHOLOGICAL CONSIDERATIONS

The basic lesion is damage to liver cells, leading to degeneration or ne-

crosis. The breaking down of bile capillaries is an expression of the damage to the functional units of the liver. This allows bile to enter the blood stream and cause the jaundice. A mild assault is usually followed by complete healing and restoration of normal function. Simultaneous destruction of all or most units is fatal. Between these two extremes are most instances of uncomplicated infectious hepatitis. Liver function tests express the various degrees of liver damage.

CLINICAL ASPECTS

There is usually a preicteric stage ranging from 20 to 120 days according to the type of infection. Increased fatigability, irritability, mild mental depression and loss of appetite may occur. Headache, chilly sensations, nausea, vomiting, upper abdominal distress, epistaxis and passage of dark urine appear.

The liver is usually enlarged and tender, the spleen palpably enlarged in a fifth of the cases. The temperature range is 99° to 103° F. The jaundice may last from one to six weeks, depending upon the degree of liver damage, and may cause itching of the skin. Edema may be noted with or without ascites in severe cases. Varying degrees of mental depression which persist after the initial infection has subsided are usual, and nervous hyperirritability lasts for a long period of time. As the jaundice fades the appetite usually reappears and recovery is imminent.

DIFFERENTIAL DIAGNOSIS

It must be determined whether the jaundice is intrahepatic, extrahepatic or hemolytic in origin. Gallbladder disease, acute appendicitis, Weil's disease, secondary syphilis and jaundices of toxic origin must be ruled out. Infectious mononucleosis may simulate viral hepatitis in onset, history and laboratory findings. Cases have been noted that progress from one disease to the other or give the appearance of one complicating the other.

LABORATORY TESTS

Bilirubinuria may be the first sign of viral hepatitis. There may also be elevation of the serum alkaline phosphatase, bromsulphalein retention, a positive cephalin flocculation test and leukopenia or leukocytosis. During the icteric stage the cephalin flocculation and thymol turbidity tests are usually positive. There is a rise in the serum alkaline phosphatase and the serum bilirubin is elevated, with positive direct and indirect Van den Bergh tests. The icterus index may be elevated from 15 to 50 or higher. There is decrease in the cholesterol esters and a marked increase in total cholesterol. The blood prothrombin time is usually decreased while there may be marked to mild bromsulphalein retention.

In severe cases total proteins may be depleted with alteration of the albumin-globulin ratio. There is a marked increase in both the urinary and fecal urobilinogen. The sedimentation rate increase is a guide to the severity of the disease and later to the improvement of the patient. There may be an accompanying hypochromic anemia. The serum transaminase provides a rough index of injury to heart muscle and liver cell. The C-reactive protein and the zinc sulfate turbidity test are also useful diagnostic guides.

TREATMENT

The basic treatment for this condition is rest. In the weeks of con-

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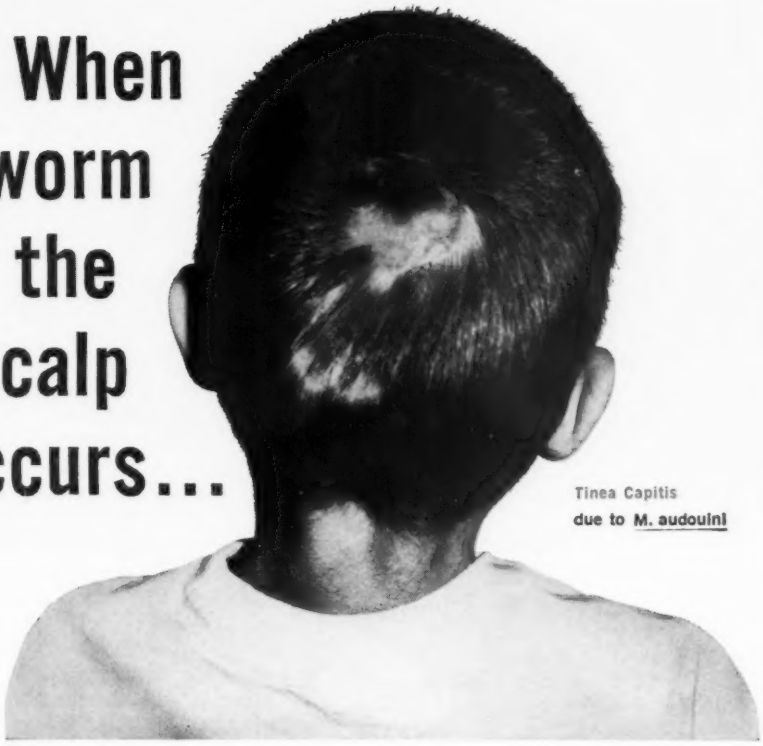

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valescence there is gradual return of strength, appetite and sense of well-being. Mental sluggishness and mild depression are probably the effects of the elevated bilirubin on the nervous system. In severe cases the convalescence is slow, with low tolerance to exercise and occasional exacerbation of symptoms. Premature return to work or activity may result in headache, malaise, arthralgia and a recurrence of distaste for food. Jaundice may return and necessitate further rest. A bland diet with high-protein, high-carbohydrate and low-fat should be encouraged. The patient who is acutely ill should be hospitalized.

Glucose and hard candy should be taken in large quantities, together with the intravenous administration of 10 per cent glucose in water (2,000 to 4,000 cc.). Vitamin K is specific for prothrombin time depletion. Whole blood is sometimes of value.

The corticosteroids are given to reduce the acute inflammatory reaction and lower the serum bilirubin in the severe icteric stage, particularly in the complicated cases. The tetracyclines seem to have some effect in preventing occurrence of secondary infection. The antihistamines are of value for itching of the skin.

Dimenhydrinate and pyridoxine hydrochloride allay nausea and have a sedative effect. All the vitamins, including B_{12}, and the lipotropins should be used if nutrition has been particularly poor; alcohol should be prohibited and allowed only in small quantities after return to normal.

The patient should not be subjected to fatigue for a period of six months. Activity may be gradually resumed after the liver is down to practically normal size, the cephalin flocculation and thymol turbidity tests are no more than weakly positive, and the bromsulphalein test shows no more than 8 per cent retention after 45 minutes. Routine laboratory checks should be done at three to six month intervals after return to work.

One attack of viral hepatitis confers immunity to the homologous virus. Prophylactically, gamma globulin has been shown to be effective in those who have been exposed to infectious hepatitis. It is reportedly of no value in the prophylaxis of serum hepatitis.

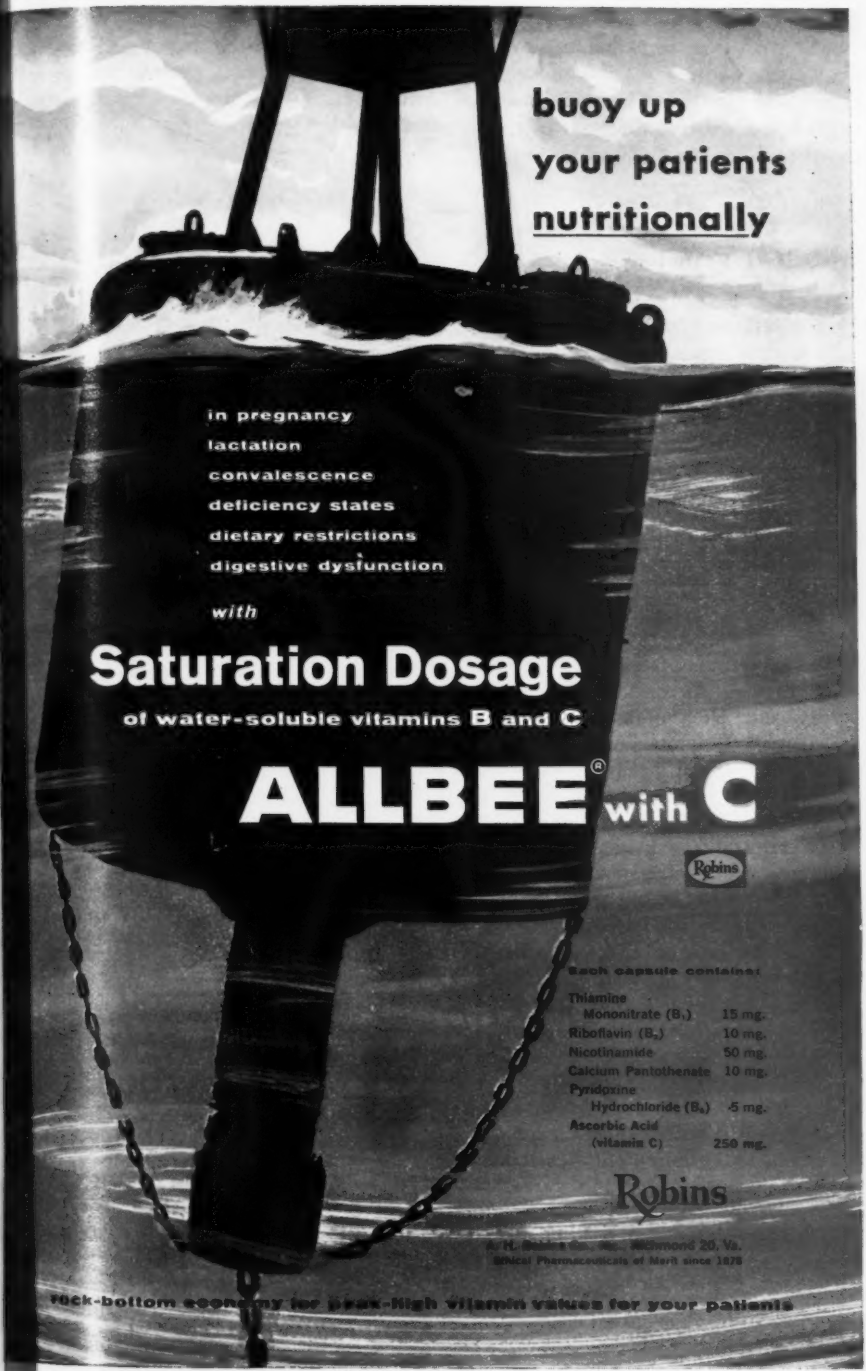
PROGNOSIS

The average morbidity of viral hepatitis is about four months; the fatality rate is less than 0.5 per cent. Persons up to 30 years of age are most susceptible. The disease may result in relapsing viral hepatitis, chronic hepatitis, the carrier state, post-hepatic syndrome and hyperbilirubinemia. Some acute cases have become chronic and gone on to coarse nodular cirrhosis.

Many cases of subclinical hepatitis present a history of lassitude, anorexia, malaise, arthralgia and mild mental depression. These may show no liver enlargement but may exhibit positive cephalin flocculation and thymol turbidity tests, with elevation of the blood cholesterol and sedimentation rate. Unless these studies are made, the diagnosis may be missed completely.

SUMMARY

A brief, comprehensive survey of viral hepatitis has been presented. The disease presents a problem to the practitioner because of its high rank among communicable diseases and its long morbidity. The importance of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the recognition of subclinical cases as well as acute cases is emphasized. The most useful of the liver function tests are discussed, methods of treatment reviewed and particular emphasis is placed upon the use of corticosteroids. The importance of regular clinical testing during convalescence is stressed.◀

Condensed from *Medical Annals of the District of Columbia*, Vol. XXVI, No. 12, December, 1957.

Assaultive Behavior in the Aged

The aggressive behavior of the aged person suffering from senile brain disease is a recognized entity, but little attention has been paid to the extreme degree of assaultiveness which leads to antisocial actions and to conflicts with the law. During a period of seven years, 327 patients charged with serious assaultive actions were referred by the courts for psychiatric evaluation. Since almost 10 per cent of such aggressive crimes had been perpetrated by elderly persons, further consideration is indicated.

The early manifestations of organic brain disease are often emotional in nature, and the depressed, agitated, and paranoid manifestations of senile or arteriosclerotic brain disease frequently come first to the attention of the court rather than the physician. The tendency to deny illness is a frequent manifestation of organic brain disease.

Two patients showed signs of arteriosclerotic parkinsonism. One stabbed his wife because she did not give him a cup of coffee, the other shot his wife then rationalized his crime by stating that she did not help him in the bathroom. A few days later the patient became rigid and developed bed sores. It seemed almost incredible that this handicapped person had been able to commit the homicidal act. Patients with parkinsonism—whether encephalitic, idiopathic, or arteriosclerotic—are unable to curb their impulses, and there are strong suicidal tendencies. The degree of motor incapacity which simulates harmlessness is deceiving.

To counteract the elderly person's feelings of uselessness, special community services for old people should be organized, and creative activities should be stimulated in people who have the resources for it. Removal of social pressures, lifting the feelings of responsibility, and inspiration of a sense of group identification might prevent emotional disturbances in the elderly and save them from court hearings and/or certification into state hospitals.

Of the 327 patients charged with felonious assault or homicidal actions, 30 (almost 10%) were in the older age group, and 18 cerebral arteriosclerotic patients were over 60 years of age. There were two cases of arteriosclerotic parkinsonism. The oldest patient (a woman) charged with homicide was 82. Only nine of the 30 patients showed the typical organic brain syndrome of severe confusion, disorientation, and intellectual deterioration. The majority of these patients were not deteriorated intellectually and revealed only emotional disturbances, and there was occasional difficulty in establishing a diagnosis of a commitable psychiatric disorder for court disposition.

Winkler, G. E., & Rosner, H., *New York State J. Med.*, 58:515-519,1958.

Masking and Gowning in Newborn Nurseries

A controlled experiment in two newborn nurseries yielded some surprising information about staphylococci

JOHN O. FORRAR, M.C., M.B., F.R.C.P. Ed., and A. F. MACCABE, M.D., D.P.H., *Edinburgh, Scotland*

Staphylococcal infection of the newborn infant is a widespread problem in maternity units, a problem to which no easy solution is apparent. Prophylaxis rather than the treatment of established lesions is the prime objective. Between one maternity unit and another, masking and gowning can vary from a strictly regulated and conscientiously performed regimen to a meaningless ritual or mere gesture.

In a maternity unit of 50 beds, two nurseries were set aside for a controlled experiment over a period of three months. At birth, babies were allotted at random to one of the two nurseries. In one nursery a strict masking and gowning regimen was in operation, in the other no masks or gowns were worn. All personnel entering the masked nursery donned a mask and gown. The masks consisted of four layers of gauze with a Cellophane insert and extended below the chin. The nursing staff changed their masks at least every hour. The masks were autoclaved in a drum and removed from the drum with sterile forceps. The instructions were that while being worn the mask should not be touched by hand. On discarding, the masks were dropped into a lidded receptacle containing antiseptic. Gowns donned before entering the nursery were put on in an

ante-room, where they were kept hanging when not in use. In addition to the gown worn on entering the nursery each cot carried a folded gown which was worn when the baby in that cot was being handled. All gowns were changed every 24 hours or when soiled. They were not autoclaved, but at one stage of the laundering temperature of the washing water was raised to 200° F. for 10 minutes. In the unmasked nursery, nurses wore their ordinary uniform, the apron of which was changed daily or when soiled.

For the first two days the babies were taken to their mothers for feeding. The mothers of the babies from the masked nursery were masked and gowned with the baby's "individual" gown. Thereafter the mothers fed their infants in the nurseries, and again in the masked nursery they were appropriately masked and gowned. Mothers were permitted to handle their own babies only. If any baby developed an infection in either nursery he was immediately removed to an isolation nursery. The babies from the masked nursery were bathed in a bathroom kept for them only while those in the unmasked nursery were bathed in another bathroom. Bathing was carried out daily from the fourth day.

As far as possible, other factors were kept constant in the two nurseries. The rule that hands should be washed between handling each baby applied in both. Daily cleaning by wet mopping was carried out in both. Temperature, floor space per cot and ventilation were the same.

Between occupants, cot clothing was dealt with as follows: The cot mattress was aired unless the baby had suffered from an infection in which case the mattress was autoclaved. Blankets were washed at 90° F. Other cot clothing, mattress cover, canvas bassinet, sheet, wrap, gown, napkin, and cot cover underwent a stage in laundering in which they were washed at 200° F. for 10 minutes.

This experiment was carried out at a time when a high infection rate for staphylococcal infection prevailed among the babies. All infections in babies, no matter how trivial, were recorded, and if possible a swab was taken from the lesion. Each baby had an eye swab taken routinely on the fourth day, a nasal swab taken on the eighth day, and an umbilical swab taken at the time of separation of the cord. Nasal swabs were taken from the staff four times during the period of the experiment.

The total number of babies admitted to the nurseries during the course of the experiment was 82 to the masked nursery and 85 to the unmasked nursery.

The mean duration of stay in the masked nursery was just over 8½ days, the range one to 16 days. In the unmasked nursery the mean was 9, the median 10, the range two to 16 days.

In this experiment we were concerned only with the effect of masking and gowning on the dissemination of staphylococci. Quantitatively, there is no doubt that staphylococcal infection is the most important one affecting the newborn infant in maternity units.

The masking and gowning regimen employed was as elaborate as is likely to be practicable in most maternity units. It was certainly more thorough than is practised in many. Yet results show no difference in the rate

of staphylococcal infection or in the staphylococcal carriage rate in the masked as compared with the unmasked nursery. At a time when the neonatal staphylococcal infection rate in the unit was high, masking and gowning failed to exert any significant effect in reducing it.

Comparison of the drug-sensitivity patterns of the staphylococci found on the babies in the masked and unmasked nurseries and on the nursing staff probably gives a clue to the ineffectiveness of masking. In the unmasked nursery there was nothing to stop the free dissemination of staphylococci from the nose and mouth of the nursing staff to the babies should such occur naturally; yet the pattern of staphylococci found on the babies differed from that found on the nurses. This suggests that little dissemination from mouth and nose of nurse to baby did in fact take place. The interposition of a mask between nurse and baby in the masked nursery would therefore not be expected to accomplish anything, and it did not. The same nursing staff served both nurseries. If the predominant spread of infection was from baby to baby indirectly, our results would be more easily understood.

In the two nurseries the same proportion of infants suffered from minor staphylococcal infections. The sites of occurrence of these infections were predominantly the eye and skin, and the umbilicus.

The carriage rate for staphylococci in the babies in the two nurseries was determined by examining swabs from the eye, nose, and umbilicus. The carriage rate for staphylococci in the attendant nursing personnel was determined by nasal swab. There was no significant difference in the carriage rates for babies in the masked and unmasked nurseries, or between the babies and the attendant personnel.

There was no significant difference in the drug-sensitivity pattern of staphylococci isolated from babies in the two nurseries, but there was a significant difference in pattern between babies' and nurses' staphylococci.

It is concluded that direct transfer of staphylococci from the nose and mouth of attendant personnel to the baby is not an important means of infection of the latter, and that masking and gowning in maternity nurseries is unlikely, therefore, to be an effective preventive measure.◀

Brit. M.J., 1:76-79,1958.

Verac

"...noteworthy effectiveness in cases of constipation induced or aggravated by anticholinergic and ganglionic blocking agents."*

*Gasster, M.: Med. Times, to be published.

STANDA

Common Precancerous Lesions

Precancerous lesions may occur anywhere in the human body. Some of the common forms are discussed

ARTHUR PURDY STOUT, M.D., *New York, New York*

Proliferations leading to invasive squamous-cell carcinomas in connection with coal-tar irritation were first observed in the skin of chimney sweeps in the 18th century. Since then heat, x-rays, the actinic rays of the sun, ingested arsenic, etc., have produced atrophies and hyperplasias which have been recognized as precancerous lesions. Pigmented moles and senile hyperkeratoses have also been recognized as precancerous.

Hyperplastic proliferations that must be considered precancerous may occur in any of the many mucous membranes that are covered with stratified squamous or transitional epithelium. A squamous-cell carcinoma developing in the conjunctival mucosa or in a senile hyperkeratosis in the skin has very little chance of becoming a metastasizing cancer that can kill. On the other hand, a squamous-cell carcinoma developing in a syphilitic leukoplakia in the tongue may be expected to metastasize in 80 per cent of cases unless it is eradicated completely and early. Carcinoma *in situ* of the cervix is often detected eight to 10 years earlier than invasive cervical carcinoma. In the larynx, however, non-invasive and invasive carcinoma are recognizable at approximately the same time.

The cancerous process in the surface epithelium may progress downward through the ducts and into the gland acini without transgression of

the basement membrane. This is not to be considered invasive carcinoma unless there has been a rupture of the basement membrane, with invasion of the substantia propria.

The term carcinoma *in situ*, or preinvasive carcinoma, has also been applied to localized carcinomas in certain glandular organs and glandular mucous membranes. The best known of these are the adenomatous polyps and papillary adenomas of the gastrointestinal tract and especially of the colon and rectum. The common papillomas of the bladder are preinvasive cancers. In the stomach, in addition to adenomatous polyps, there may be certain atrophic changes such as those associated with pernicious anemia and the more common lesion of the older years of life in which, by a process of metaplasia, the gastric glands are changed into glands of an intestinal type. Both of these changes have been regarded by many observers as precancerous. In the female breast, certain intraductal proliferative changes in cystic disease contribute three or four times the incidence of carcinoma than is the observed breast cancer incidence for the average woman of comparable age. Another less commonly observed lesion in the female breast, lobular carcinoma *in situ*, is cancerization of ducts and their acini and is comparable with cervical and laryngeal carcinomas *in situ*.

Finally, actual or probable carcinomas that occur in glandular organs may not metastasize at all, or only after a very long time. Adenomas of the kidney and liver are less common examples of this group. The small glandular proliferations in the prostate have been called latent carcinomas when they have been discovered either by biopsy or at autopsy. They are present with increasing frequency in men of advanced years and they were found in 90 per cent of men at or past the age of 90 years. Some of these microscopic tumors have metastasized before their presence was clinically demonstrated by biopsy.

Of preinvasive carcinoma of the cervix uteri, the many and varied lesions of the skin known to be precancerous, and adenomatous polyps and papillary adenomas of the rectum and colon, more is known and written than about any of the other recognized precancerous proliferations. Others are all too common. Latent carcinoma of the prostate probably exists in 16 per cent of men over 40 years of age. Carcinoma *in situ* in the tracheobronchial tree is very common in men, especially in those who have been heavy cigarette smokers and in those who have invasive bronchial carcinoma. The papillomas of the bladder which frequently lead to invasive carcinoma are common also. The atrophic changes in the gastric mucous membrane with intestinal metaplasia may be a harbinger of invasive cancer.

Many of the intra-epidermal and intramucosal carcinomas *in situ* desquamate cancer cells so that they may be obtained from smears or washings of those surfaces. When tumor cells are desquamated it is usually not possible to tell whether they come from invasive or non-invasive carcinomas. In a great majority of instances they are cast off by a carcinoma that has already invaded, and these are not the subject of this discussion. Only in the cervix uteri does the discovery of abnormal or cancer cells in the smear usually lead to the


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*Biegeleisen, H. L.: Clinical Medicine; Oct., 1955
*Roberts, J. T.: Clinical Medicine; Nov., 1957

detection of preinvasive cancer. This examination may give the first indication that there is an unsuspected invasive or non-invasive carcinoma and, if positive, calls for immediate extensive biopsy of the mucosa of the cervical canal.

Nieburgs et al. recently screened practically all of the women above the age of 19 years living in Floyd County, Georgia.

This meant 27,894 examinations of 17,761 women over a period of four years. The prevalence rate of carcinoma *in situ* was found to be 2.8 per thousand women, for invasive carcinoma 1.4 per thousand. It also showed that in every thousand women 1.8 new cases of cervical carcinoma *in situ* developed each year. When carcinoma *in situ* of the cervix is followed without treatment, Peterson has shown that after one year invasive cancer will have developed in four per cent, after three years, 11 per cent, after five years, 22 per cent, and after nine years, 33 per cent.

PRECANCEROUS LESIONS IN VARIOUS PARTS OF THE BODY

What to do about precancerous lesions in various parts of the body is not easy to decide. For the cervix lesions the uterus can be removed and the danger of both infiltrative cervical and endometrial cancer eliminated. But what shall be done about cystic disease of the female breast? Only complete bilateral mastectomy will take away all possibility of breast cancer. There is an increasing tendency to recommend total colectomy when there are three or more polyps, with or without cancer *in situ* because of the danger of more polyps of the colon developing and of subsequent carcinoma with invasion. From an analysis of the follow-ups on many cases with three or more polyps on which total colectomy was not done, Grinnell and Lane have found that these patients would not have been benefited by this radical procedure.

At the present time many precancerous lesions in different parts of the body are recognized, but in most instances we can think of nothing more effective than to remove the individual lesion or the organ or tissue in which it is found. This is feasible for the uterus, but impossible for single vital organs like the liver and pancreas or for paired vital organs like the lung, and of highly questionable propriety for paired non-vital organs like the female breasts. In a few instances etiologic agents are known, and when they occur in industry, steps can be taken to protect those exposed to them. The same is true of overexposure to roentgen rays.◀

Pennsylvania M.J., 61:481-483,1958.

Ivy Poisoning

"Ivy poisoning" is a term applied to skin irritation resulting from contact with any one of more than 60 varieties of plants found in the United States. It is a year-round hazard most common during summer. Most persons are immune to the biggest share of them, but nearly everyone who touchs the three more commonly known plants—poison ivy, poison oak and poison sumac—is affected to some degree.

Ivy poisoning is caused in four ways: Bodily contact with any part of the plant, exposure to smoke from the burning plant, contact with clothing or other objects that have been exposed to it, and wading or swimming in water containing its oil.

The National Safety Council, *The Health Bull. (N.C.)*, 73:10,1958.

FINANCE

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

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These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many businessmen. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

One of the oldest maxims of investing is to look before you leap. One translation of this into practical terms is that you must examine all the aspects of a company before you consider investing in it. Such an examination, of course, involves a much more detailed study of the situation than just a superficial examination of the earnings in the latest year, for one year's financial statements rarely tell the whole story about a company.

There are many reasons for this. Some have to do with the corporate tax laws. Occasionally a company will appear to be selling at a strikingly low price-times-earnings ratio (one of the most widely used analyti-

cal tools), but on closer inspection, it will be seen that the company is not paying any income taxes in a given year because it has a tax-loss carryforward, which might expire the following year. An unusually low price-earnings ratio may also be caused by a large potential dilution factor (a large convertible bond issue, or a big granting of options outstanding, which if exercised would greatly increase the number of shares outstanding).

Unusually high yields often have explanations, too. In many cases, of course, a yield (the dividend as a percentage of the price of the stock) far higher than is traditionally the case for the company often means that the dividend is in danger.

The three issues we will discuss this month are undervalued at present levels for reasons which escape first glance but which are strikingly revealed upon more detailed analysis. The first, General Bronze Corp., is a firm which has been tied to the residential building industry for many years but which is now on the verge of transforming itself into an electronics company with sharply enhanced earning power. The second, Peerless Insurance Co., appears to be a reasonably priced stock on its own without giving any weight to its ownership of most of the stock of a rapidly growing life insurance company whose accounts are not consolidated with those of the parent company. The third, Eaton Mfg. Co., is an auto parts maker whose shares, in our opinion, are overemphasizing the effects of the auto recession, and not giving enough weight to the proven earning power the company will display in bigger auto years.

GENERAL BRONZE CORPORATION

General Bronze Corporation is a perfect example of why an investor must look behind the figures. Certainly the 1958 earnings to date do not look promising. Nonetheless, we look for a sharp increase in earnings next year and consider the stock definitely under-valued. General Bronze Corporation was incorporated in 1927, and over the next three decades acquired several other firms. The company is the largest producer of aluminum windows and aluminum window accessories and architectural metal work in the United States. It now operates through four divisions and a subsidiary.

During 1957, approximately $16 million of the company's total of $25 million in sales was divided among the Permatite and the Alwintite divisions. Low cost aluminum windows, screens and storm sash windows are sold under the name Alwintite, while custom built metal windows are sold under the Permatite trade name.

Approximately $3.6 million in sales was accounted for by the Brach and Steel Weldments divisions. The Brach Company manufactures antennas for several automobile companies, while the Steel Weldments division is a metal fabricator under contract for other companies.

A little publicized division now, G B Electronics, had sales of $5.7 million last year. It is this division, however, that we feel will produce a major change in the operations of General Bronze.

Although established only 6 years ago with three people, G B Electronics is now at a point where it employs nearly 200 scientists, engineers and technicians. Its importance can be readily recognized when it is noted

that sales in the foreseeable future of this division should equal the $25 million achieved by the entire General Bronze Corporation in 1957. In order to more fully exploit these opportunities, General Bronze only recently established G B Electronics, formerly a division, as a wholly-owned subsidiary. Also the company has leased a new plant encompassing some 160,000 square feet of manufacturing space at Valley Stream, Long Island. This site will be occupied this month, and the plant will employ several hundred people.

G B Electronics produces equipment currently in urgent demand, particularly with the growing emphasis on missiles. The subsidiary is one of the nation's largest manufacturers of radar antennae and associated components. The demand for radar has risen sharply due to the rapid gains in technology which permit more effective detection and give greater range. In recent years, a new radar technique has been developed which permits detection of flying objects thousands of miles away from the source. This new "super-radar" is slowly reaching the production stage and should lead to a sharp increase in sales. The super-radar is an obvious defense necessity in detecting intercontinental missiles, and the development will make older facilities, such as the much-publicized "DEW Line," obsolete. Another method of detection, known as Infra-red, utilizes heat rays given off by substances. The company also has an important stake in this area.

In order to establish a major position in the electronics industry, General Bronze's management several years ago correctly decided to substantially step up research expenditures in military electronics. In the years 1955 through 1957, approximately $1 million a year was spent on research. The magnitude of these expenditures is obvious when it is realized that such outlays approximated $2.50 per share before taxes in each year.

The substantial sales increases which may be anticipated in the immediate future are due largely to the success of these research expenditures in developing a proprietary line of antennae. The technical competence and strong competitive position is further demonstrated by the development of an entirely new antenna shape as contrasted to the familiar parabolic antennae. The new technique, known as SVE (swept volume efficiency) is reputed to offer similar performance with smaller size, less weight and reduced cost.

The equipment produced by this subsidiary, in addition to the radar and scatter communication antennae, include radio telescopes, missile tracking antennae and other radar high frequency components. This equipment is sold to a broad section of electronics companies. While no recent backlog figures have been announced, a trade publication recently reported that a contract of approximately $20 million will be awarded the company.

The Alwintite division, which accounted for nearly a third of 1957 sales, is the nation's largest manufacturer of sliding glass aluminum windows and aluminum doors. Sales are bolstered by the use of the products in many prefabricated home buildings, including the products of National Homes Inc. and American Houses, Inc. This division is influenced principally by changes in the

level of residential construction. Through 1955, sales expanded materially, but in 1956 and 1957 sales dipped rather drastically due to the decline in home building.

The Permatite division is a leading manufacturer of the well-known curtain wall system used in large multistoried commercial buildings and schools. The company utilizes bronze, aluminum and stainless steel in its manufacture of these wall panels. As a pioneer in developing the curtain wall method, the company has obtained a major share of the business. Buildings which have already used curtain walls include the Lever House and the Seagram Building in New York, as well as numerous office buildings and apartment houses. The largest contract ever let in this field was given to the Permatite division for the new Chase-Manhattan Bank Building which will be erected this year.

The past earnings record of General Bronze has been erratic, mainly reflecting changes in building activity. During 1950, a year of record construction activity, the company had record profit margins in earnings, with sales of approximately $20 million while net income came to $4.07 per share. Although the company was able to increase sales to a level of approximately $30 million for 1951 to 1955, earnings fluctuated between $4.04 a share in 1951 and $3.34 a share in 1955.

With a reduction in military spending and the reduced rate of residential construction, both earnings and sales declined in 1956 and 1957. In 1957, sales dipped to the lowest level since 1952, slipping to $25.3 million. Earnings dipped to $2.01 a share in 1957, down slightly from the $2.02 a share earned in 1956.

With a record demand for curtain walls from several major building projects and an improvement in the military end of its business, the backlog totaled $28 million in March 1958. Deliveries in the first quarter were $6.2 million, compared to $6 million in the like period of 1957. Earnings also improved modestly, rising to 51¢ a share from 50¢ in the same first quarter of 1957.

Unfortunately, the improvement did not hold in the second quarter of 1958. Due to factors which could not be controlled by the company, deliveries on some of their building projects were delayed, and roughly $7 million in contracts was deferred. Earnings during the quarter slipped to 18¢, far below the 64¢ earned in the same quarter of 1957, and brought earnings for the half to 69¢, compared to $1.14 a share in the first half of 1957. Earnings during the balance of the year are not expected to be much above the 87¢ reported in the second half of 1957, and as a result earnings this year are likely to be somewhat below the $2.01 a share reported last year.

The very factors which are making 1958 a relatively poor year will serve to stimulate the company's position in 1959, however. Permatite's deliveries, which are currently being deferred, will be that much more important in 1959. In addition, the recent easing of mortgage credit has greatly improved the outlook for residential building. As a result, the company's Alwintite division currently is improving its position and should contribute importantly to earnings in 1959.

Based on these anticipated improvements, the company in 1959 will

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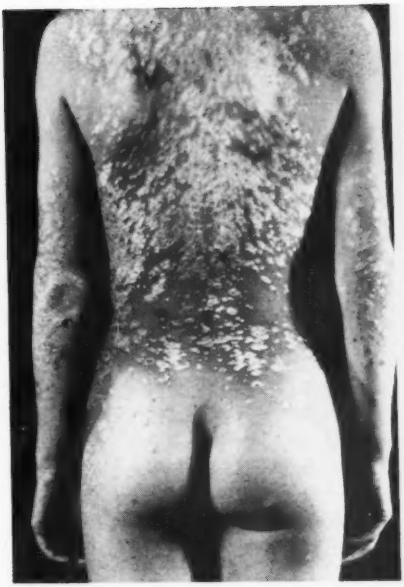

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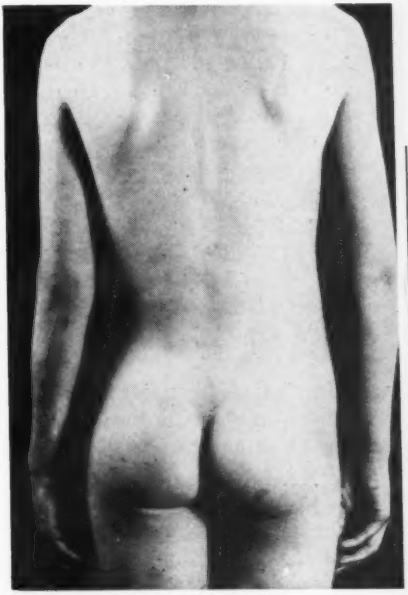

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General Bronze Corporation			
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Dividend	$1.50	Long-term Debt	$2,400,000
Yield	5.4%	Common stock	380,377 shs.
1958 Price Range	31⅜-19⅛		
Traded	N.Y.S.E.		

be in a position to at last equal the record earnings of $5.07 a share reported in 1950. Once more, the basic position of the electronics industry should be sufficiently strong to permit an improvement in volume for a number of years thereafter due to the country's military build-up in missiles. Furthermore, the company's strong research organization, which has already developed a substantial business, should continue to contribute importantly to widening the sales base.

The financial condition of the company is strong and we believe the substantial expansion anticipated in the months ahead can be financed entirely through internal sources. Even though earnings of 1958 are likely to be below those of 1957, we nevertheless look for a maintenance of the current $1.50 dividend rate. At a future date, when earnings are at the much higher plateau discussed above, we would expect increases in the dividend payments.

In view of the major improvements underway, we think the shares can be bought as an interesting speculation.

PEERLESS INSURANCE COMPANY

In our opinion, the shares of Peerless Insurance Company are clearly undervalued in relation to their basic intrinsic worth. An important consideration in the evaluation is the ownership of most of United Life and Accident Insurance Co., which is an extremely fast growing firm. Investors appear to have overlooked a good deal of the value inherent in this situation because the financial accounts of this subsidiary are not consolidated with the parent company.

Peerless Insurance was incorporated in 1901, and added fire and inland marine lines in 1950 to supplement the writing of a wide variety of casualty and bonding coverages. In December, 1956, Peerless acquired the American business of the Caledonian Insurance Company of Edinburgh. Financial control of United Life & Accident was acquired in May, 1952. As of December 31, 1957, Peerless owned 15,896, or 78.98 per cent of the 20,000 shares of United Life presently outstanding. Furthermore, the company holds options to buy an additional 2,657 shares at $150 per share. Purchase of these shares would increase the total Peerless holdings in United Life to 92.26 per cent.

Last year, Peerless did $14.3 million in net premiums, divided 60 per cent among automobile and other casualty lines, 26.1 per cent in fire, inland marine and miscellaneous lines, 9.4 per cent in fidelity, surety and burglary and 4.2 per cent in accident and health. The company is licensed and operates nation-wide, as well as in Canada and Puerto Rico.

Underwriting profit margins and earnings for Peerless, as for most fire and casualty companies, have fluctuated widely but in the main have pro-

duced satisfactory results. In the 1953-1955 period, for example, the combined loss and expense ratio was 93.5 per cent, which produced excellent underwriting profits. However, in 1956, due to a sharp rise in Workmen's Compensation losses, automobile bodily injury liability and automobile physical damage claims, as well as poor return from surety business, the overall loss ratio jumped nearly 19 points to 68.7 per cent of premiums. The combined loss and expense ratio soared to 112 per cent producing a statutory underwriting loss of $3.2 million.

In 1957, however, this trend was reversed and a small statutory underwriting profit of $140,000 was reported. After adjusting for this decrease in the unearned premium reserve and for a tax rebate, combined earnings, excluding any equity in the earnings of United Life & Accident, came to $2.06 a share in 1957. This compared with an adjusted loss of $1.73 a share in 1956 and earnings of $2.38 a share in 1955.

The company's net investment income has grown steadily from the 83¢ of 1953 to $1.35 a share in 1957. Last year, investment operations were influenced by unusually large requirements for cash which resulted in a reduction of $1.7 million in the company's investments.

United Life & Accident Insurance Co. is authorized to write life, health, casualty, liability and indemnity insurance, but at the present time does only a life and accident and health business. Insurance is written both on the non-participating and participating plans. However, so far almost all the insurance written has been non-participating, which has special significance to stockholders since all profits on this type of policy accrue to stockholders.

Growth of United Life has been very rapid, especially since the company was acquired by Peerless. This year, management expects to show an increase of life insurance in force by 15 per cent, which would be double what the industry as a whole is projecting. In the last five years, for example, life insurance in force has climbed from $156.9 million to $282.4 million, while premiums earned have climbed from $3.7 to $5.6 million.

In 1957, United Life & Accident reported a net operating loss of $53,000, compared with a gain of $48,000 in the previous year. This, however, is not the full story. In the life insurance industry, new business put in force reduces the company's surplus and penalizes net income because first year premiums on a policy are not as large as the amount necessary for the company to pay (or set aside as reserves) during this period. For example, during 1957, the acquisition cost of direct ordinary new life insurance amounted to $10.05 per $1000 of insurance in excess of first year premiums. The company feels that a cost of less than $15 per $1000 of new business is an excellent investment, since this same amount of insurance in force has a present value (in that it could be sold by the company) of $20 per $1000 of insurance, or more.

Dividends are currently being paid on Peerless shares at a $1 annual rate. This represents a pay-out of some 74 per cent of net investment income. The common stock has paid dividends without interruption since the company was organized, except for the year 1914.

The year-to-year fluctuations of underwriting results from fire and

Peerless Insurance Company			
Price	$26	Capitalization (12/31/57)	
Dividend	$1.00	Common stock	550,000 shs.
Yield	3.8%		
Traded	O.T.C.		

casualty operations are usually so wide and so unpredictable that earnings estimates for any one given year are extremely difficult. However, it is possible by using past records to project profit margins for 5 to 10 year periods. In view of the company's above-average underwriting operations, a projected 5 per cent profit margin appears reasonable. Assuming $15 million in premium writing, average after tax earnings from fire and casualty operations would be $1.80 to $2.00 per share.

On the basis of current price-earnings ratios in the industry, these earnings would be worth $16 to $18 in the price of the stock. Furthermore a valuation of $16-$18 would still only be about 77 per cent of adjusted book value, and only 12.6 times net investment income.

The earnings coming to Peerless from United Life, capitalized at 15 times earnings would be worth approximately $23 per share of Peerless, and on the basis of eventual 92.26 per cent ownership of United Life, would be worth $26 a share to Peerless. Moreover, we feel that a multiple of 15 times earnings seems conservative in view of the fact that other life insurance companies having comparable growth records sell, in many cases, at 20 or more times adjusted earnings.

These figures suggest a basic intrinsic worth of $39 to $44 per share. Future prospects for continued growth and profitability for both companies appear excellent. The shares are suitable for investors interested in both near and long-term possibilities and growth prospects.

EATON MANUFACTURING COMPANY

Eaton Manufacturing Company is a manufacturer of automobile parts, notably axle and engine parts for both passenger cars and trucks. Although current operations are at low levels, the company looks for a distinct improvement in the 1959 model year. The company thus qualifies as another example of the need to look behind the figures—in this case, the one bad year's earnings.

While Eaton does approximately a third of its volume in the truck field and is becoming increasingly active in other industries, including aircraft, electronics, railroad, appliances and farm equipment, the company's fortunes, by and large, run hand-in-hand with those of the automobile industry. Despite the growing trend for automobile companies to integrate their operations and produce many more parts themselves, the company makes no apologies for its identification with the industry, for it believes that by designing and engineering better, more efficient parts, keeping its plants in shape and remaining on top of costs and designs, it can be an efficient and low cost competitor with other parts makers as well as with the automobile companies themselves. Eaton recently showed its confidence in the future

of its industry by acquiring the Fuller Manufacturing Company, an important supplier of heavy duty transmissions for trucks and off-the-road equipment.

The company had long believed that it should be in the truck transmission business because of the complementary nature of axles and transmissions, and because 5 of the captive producers of automotive parts have made both transmissions and power-driven rear axles, as have three of the independent competitors of Eaton and Fuller. The benefits to each company from the affiliation should be both immediate and long-range.

The company operates plants in Cleveland, Marion and Massillon, Ohio; Battle Creek, Vassar, Cold Water, Marshall, Saginaw, Detroit and Lawton, Michigan; Kenosha, Wisconsin; North Tonawanda and Lackawanna, New York; Richmond, Indiana and Ontario, Canada. Research Laboratories are operated in Cleveland and Detroit, and a majority owned Brazilian subsidiary was formed last year.

Eaton's product breakdown last year was roughly 35 per cent axles, 30 per cent engine parts, including valves, tappets, hydraulic valve lifters and valve seat insets; 10 per cent coil and leaf springs; and 25 per cent was scattered among castings, heaters, stampings, eddy current and induction drive apparatus, power steering pumps, magnetic powder clutches and jet engine blades. The company also produces automobile air conditioners, which are largely sold through Sears, Roebuck and Company.

The company is doing development work on a number of new products. One of these is a magnetic clutch which is expected to be introduced on some foreign cars later in the year. The clutches have been in service in France, and an American manufacturer is now experimenting with them. The company hopes to be able to make an important announcement about this program in the not too distant future. Other new products which the company believes have important sales possibilities include:

1. A new two-speed tandem axle which distributes a truck load over four wheels to come within the weight laws of various states for highway loading, with the two live driving axles also providing maximum traction.

2. A limited slip differential for passenger cars and trucks which is now under test by a major customer.

3. A compact under-the-dashboard air conditioner.

In a tandem axle, two live driving axles are mounted together on a carriage supporting the rear end of a truck or tractor. Both are live axles because of the necessity of providing the maximum traction for moving the vehicle. The two speed tandem design is a new development by Eaton which gives the tandem the known and proved advantages of the wide range of a two speed axle.

The motor truck industry is also actively working on new developments which will undoubtedly change the vehicle more in the next ten years than during the past 30 years. Possibilities exist of putting engines in the rear, of using independent input-to-drive wheels and other developments.

Other new products in the works include a viscous fan drive which produces infinitely variable speeds and was originally developed for use in

EATON MANUFACTURING COMPANY

Price	49½
Dividend	$3.00
Yield	6.1%
1958 Price Range	51-38½
Traded	N.Y.S.E.

Capitalization (12/31/57)	
Long-term debt	None
*Common stock	1,838,044 shs

*Plus 458,310 shares to be issued in fuller acquisition

automotive air conditioners, and is now being adapted for other automotive applications and household appliances requiring constantly controlled speeds; plastic blower housings for heaters and air conditioners, which would put the company in an entirely new field; and a new type of pulley for use in generators, power-steering systems, fans, air conditioners and water pumps.

The company's sales and earnings since World War II have largely reflected the ebb and flow of the tide of the automobile industry's fortunes, but the company has shown definite growth over this period. Thus, earnings have risen from the 1946 level of $2.01 a share and reached a high of $7.42 a share in 1955, the record automobile year to date. Earnings then receded to $7.06 a share in 1956 and to $6.02 a share in 1957.

With 1958 one of the worst automobile years in postwar history, earnings slipped even further to $1.65 a share in the first half of 1958, down from $3.58 a share in the same period of 1957. We look for earnings for the full year to be approximately $3.25 per share. While this will be down quite sharply from the 1957 level, the quarterly dividend of 75¢ is expected to be maintained. The cash flow is high at about $12 million, with requirements of only about $5 million for capital expenditures and about $5½ million for dividends. Net working capital on June 30, 1958, was equal to $33 million, and the parent company has no long-term debt although a recently formed subsidiary has about $2 million of long-term insurance loans.

While Eaton's sales and earnings reflect the current recession in the automotive industry, the company has not cut back on its research and development expenditures and, in fact, has increased its efforts in these directions. The company is also conducting research aimed in other directions, particularly in jet engines and air conditioning. It recognizes the risks in the highly competitive automobile industry, as well as the increasing integration by the major customer companies. However, this is not a new situation and since Eaton has been able to compete successfully in the past and show a better-than-industry trend, management is confident of Eaton's future prospects and looks for a doubling in sales over the next five years. Management believes profit margins can be maintained and earnings expanded in line with this larger volume.

Despite the ups and downs of the automotive business, Eaton has paid dividends of at least $3 a share in each of the past ten years, and larger amounts when earnings warranted. These shares have appeal as a good quality issue providing an indicated yield of approximately 6 per cent, and offering longer-term price appreciation possibilities.◀

NEW PHARMACEUTICALS

Formatrix *(Ayerst)*

Each tablet contains 1.25 mg. of conjugated estrogens equine, 10 mg. of methyltestosterone, and 400 mg. of ascorbic acid. *Indications:* Specially formulated to relieve low back pain and to promote healing of fractures in osteoporosis. Aids bone matrix formation. *Dosage:* As directed by the physician. *Supplied:* In bottles of 60 and 500 tablets.

Cedesron *(Smith)*

Hematinic tablet with gastric-resistant coating for better absorption and tolerance. *Indications:* In the treatment and maintenance of the average uncomplicated case of macrocytic, hypochromic or nutritional deficiency anemia, including pernicious anemia. *Dosage:* One or more tablets daily. *Supplied:* In bottles of 30 and 100 tablets.

Polykol Drops *(Upjohn)*

Oral wetting agent. Each cc. contains 200 mg. of poloalkol (oxyethylene oxypropylene polymer). *Indications:* For the prevention and treatment of constipation associated with hard, dry stools. *Dosage:* As determined by physician. *Supplied:* In dropper bottles containing 30 cc.

Delvex *(Lilly)*

Broad-spectrum anthelmintic for oral administration. *Indications:* Destroys or eliminates four intestinal parasites: whipworm, threadworm, large roundworm and pinworm. *Dosage:* As directed by physician. *Supplied:* In 50 mg., 100 mg., and 200 mg. tablets, in bottles of 50. The 100 mg. and 200 mg. size also are provided in packages of 1,000.

Migral *(Burroughs Wellcome)*

Each tablet contains 1 mg. of ergotamine tartrate, 25 mg. of cyclizine hydrochloride and 50 mg. of caffeine. *Indications:* Allays migraine-induced and ergotamine-induced nausea while aborting the migraine attack. *Dosage:* As directed by the physician. *Supplied:* In bottles of 20 and 100 tablets.

Bonamine Elixir *(Pfizer)*

Each 5 cc. teaspoonful contains meclizine equivalent to 12.5 mg. of meclizine hydrochloride. *Indications:* For the prevention and treatment of motion sickness, morning sickness in pregnancy and the vertigo, nausea and vomiting associated with labyrinthine and vestibular disturbances. *Dosage:* As determined by the physician. *Supplied:* In pint bottles.

Kantrex *(Bristol)*

Bactericidal antibiotic for control of infections caused by both Gram positive and Gram negative pathogenic organisms. *Indications:* In the treatment of infections caused by staphylococci resistant to other antibiotics and in infections of the urinary and respiratory tract. For control of gastrointestinal tract infections caused by shigella and salmonella. *Dosage:* As determined by physician. *Supplied:* Capsules, 500 mg., in bottles of 20 and 100. Vials of 500 mg. as 2 cc. of solution, vials of 1.0 gm. as 3 cc. of solution, for injection.

Meti-Derm Aerosol *(Schering)*

Topical prednisolone spray. Each spray dispenser contains 50 mg. of prednisolone in a base of isopropyl myristate and propellant. A three-second spray delivers approximately 0.5 mg. of prednisolone directly to affected areas of the skin. *Indications:* In allergic and inflammatory conditions of the skin such as atopic dermatitis and contact dermatitis. *Dosage:* One 2 or 3 second spray 3 or 4 times daily. *Supplied:* In individual aerosol containers.

Norisodrine Sulfate Starter Set *(Abbott)*

As a convenience to patients starting on bronchial inhalation therapy. Set includes Aerohalor, vial of three *Norisodrine* cartridges, a dust-tight carrying bag and thorough instructions. *Indications:* For bronchial inhalation therapy of asthma. *Dosage:* For mild asthma, 2 to 4 normal inhalations of 10% powder. For moderate to severe asthma, 2 to 4 normal inhalations of 25% powder. *Supplied:* In individual kits.

Polaramine Repetabs and Tablets *(Schering)*

Antihistamine. Each Repetab contains 6 mg. of dextro-chlorpheniramine divided into two doses. The outer layer and inner core, separated by a timed-disintegration barrier, each contain 3 mg. of the drug. Each tablet contains 2 mg. of dextro-chlorpheniramine. *Indications*: Prevention and treatment of all allergic conditions responsive to oral antihistamines. *Dosage:* Repetabs, 1 in the morning and 1 in the evening. Tablets, 1 tablet 3 or 4 times daily.

Suitrate *(Patch)*

Antispasmodic and sedative. Each cc. contains 15 mg. of sodium phenobarbital and 2.5 mg. of methscopolamine bromide, alcohol 15 per cent. *Indications:* In the treatment of gastrointestinal disorders such as nervous indigestion, gas or belching, regurgitation, gastrointestinal cramps, abdominal pain, bloating flatulence, hyperacidity, gastric neuroses and colonic spasm. *Dosage:* Average maintenance dose for adults, 10 to 15 drops before meals and at bedtime. *Supplied:* In bottles containing 4 ounces or 1 pint.

Cortrophin-Zinc *(Organon)*

ACTH with zinc hydroxide. Each cc. contains 40 U.S.P. units of ACTH and 1.0 mg. of zinc hydroxide. *Indications:* In the treatment of rheumatoid arthritis, rheumatic fever, bronchial asthma, allergies and hypersensitivities, and inflammatory skin and eye diseases. *Dosage:* Individualized to patient requirements. *Supplied:* In 5 cc. vials.

Vistaril *(Pfizer)*

Psychotherapeutic agent. Capsules contain 25, 50 or 100 mg. of hydroxyzine pamoate. Each cc. of parenteral solution contains 25 mg. of hydroxyzine as the hydrochloride. *Indications:* For the treatment of tension and anxiety, as well as more severe behavior disturbances including the overt psychoses. Useful in aborting many acute cardiac arrhythmias. *Dosage:* As determined by physician. *Supplied:* In 25, 50 or 100 mg. capsules, and 10 cc. vials.

Ambar No. 2 Extentabs *(Robins)*

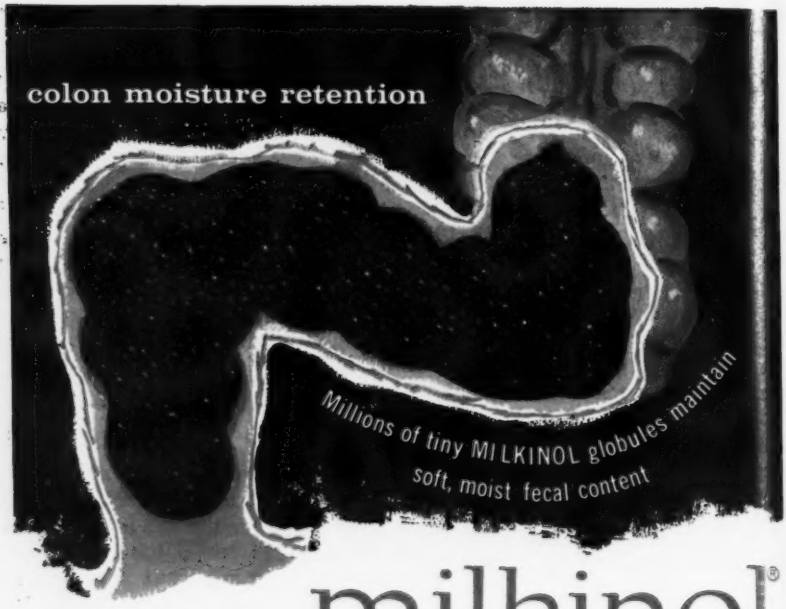
Extended-action tablets constructed to provide therapeutic effects of the intensity of ⅓ the active ingredients uniformly sustained for 10-12 hours. Each tablet contains 15 mg. of methamphetamine hydrochloride and 64.8 mg. of phenobarbital. *Indications:* For the control of obesity. *Dosage:* One Extentab before breakfast. *Supplied:* In bottles of 100 Extentabs.

Capsebon *(Pitman-Moore)*

A shampoo base containing a 1% cadmium sulfide suspension. *Indications:* For the treatment of seborrheic dermatitis of the scalp. *Dosage:* Use as shampoo, then reapply and allow to remain on hair a few minutes. Rinse. *Supplied:* In plastic squeeze bottles.

Belbarmine *(Charles C. Haskell)*

Controls appetite and elevates the mood. *Indications:* In obesity and tension-anxiety states. *Dosage:* One tablet 2 or 3 times daily as directed by physician. *Supplied:* In bottles containing 100, 1000 and 5000 tablets.



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Milkinol, a unique aqueous-mixing liquid petrolatum, assures soft, moist fecal content by retaining colon moisture balance—solves the constipation problem for all age groups, even chronic constipation of long-standing.

Uniform retention of Milkinol within the fecal mass avoids leakage. There is no interference with nutrition or vitamin absorption when taken as directed.

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briefs: MEDICAL

Malignant Hemangioendothelioma

Two cases of primary hemangioendothelioma of the liver and one case of primary sarcoma of the liver have been the only instances of primary malignant tumors of the liver of mesenchymal origin in more than 10,000 autopsies, performed over a period of 30 years.

The two patients' main complaints were abdominal swelling, shortness of breath and weakness. Case 1 had dark urine and light stools, abdominal pain and weight loss and a history of heavy alcoholic indulgence. Both patients had hepatomegaly and ascites, without splenomegaly. Case 1 also had icterus spider angiomata and gynecomastia. Since this patient was found to have coincidental portal cirrhosis, these symptoms may be understood on this basis alone. Case 2 was complicated by a mass in the left breast with left axillary node enlargement and clinical signs of a right-side cerebrovascular accident. Both showed hyperbilirubinemia, positive cephalin flocculation and a slightly elevated alkaline phosphatase. Case 1 also manifested reversal of the A/G ratio, increased bromsulfalein retention, high thymol turbidity and increased urinary urobilinogen. Case 2 had a severe anemia, a moderate leukocytosis with a shift to the left, an unexplained severe thrombocytopenia, and a lesion of the left 6th rib which was correctly interpreted clinically as a metastasis. In neither of the two cases was the diagnosis of hemangio-endothelioma entertained clinically.

Bloch, C., *J. Mt. Sinai Hosp.*, 25:115-127,1958.

Considerations in Allowing Air Travel

Among the disease conditions that do not contraindicate air travel are: Fully compensated valvular heart disease where pressurization is afforded above 9,000 feet. If the patient is decompensated and dyspneic on exertion, air travel may be permitted if under 100% oxygen all the way.

If anginal pain is brought on by slight exertion, the patient should not travel by air. Coronary thrombosis patients should not fly within six weeks thereafter. Such patients who are ambulatory may fly, if oxygen is available at all times.

Ordinarly, hypertensive patients do well in air travel. Mild preflight sedation is needed for most hypertensive patients.

Persons with mild cases of asthma may travel by air between attacks. Any condition causing dyspnea on slight exertion contraindicates flying. Patients with foreign bodies in the lung may be flown, if oxygen is available at all times.

Hemoglobin below 60% is a relative contraindication. Oxygen should be available at all times. Leukemic pa-

tients should be given a transfusion before, and have oxygen available during, flight.

Diabetics may be flown if they need no insulin during the time in air. Those who administer their own insulin may fly at any time.

Peptic ulcer is no contraindication.

Those with large unsupported hernias should not be accepted.

Nervous patients may be carried if given a sedative beforehand and the stewardess should be notified to continue necessary sedation in flight.

Brain tumors, epilepsy and palsy usually do not contraindicate air travel. Cases in which bowel or bladder control is lacking should be rejected.

Kidera, G. J., *New York J. Med.*, 58:853-858,1958.

Reliability of Electrocardiographic Diagnosis of Left Ventricular Hypertrophy

The presence and degree of left ventricular hypertrophy found at autopsy on 550 patients, and from whom electrocardiograms were made during life, were correlated with the electrocardiographic findings in these patients. The ECG diagnosis of left ventricular hypertrophy had been made in 108 patients, confirmed by autopsy findings based on heart weights in 75 patients, and not confirmed in 17. A careful analysis of the findings in the 17 patients with normal cardiac weights disclosed that in none of these was there a known cause for cardiac hypertrophy, nor was there significant cardiac disease.

The findings suggest that presently available ECG criteria for the diagnosis of left ventricular hypertrophy appear to be moderately satisfactory, to be accepted as an expression of probability rather than as a diagnosis.

Selzer, A., et al., *Circulation*, 17:255-265,1958.

the new concept

Anergex*

the injectable which inhibits the **allergic response**

A single short course of injections—1 ml. daily for 6-8 days—provides prompt relief which persists for months in most patients, and can be maintained by occasional booster doses.

Anergex therapy suppresses allergic manifestations, regardless of the offending allergen, thus eliminating skin tests, special diets, and long drawn-out desensitization procedures.

Over 500 documentated case reports[1,2,3,4,5] show that Anergex provided marked improvement or complete relief in over 60 per cent.

Anergex is effective in: seasonal and nonseasonal rhinitis (pollens, dust, dander, molds, foods); allergic asthma; asthmatic bronchitis and eczema in children; food sensitivities.

Available: Multiple-dose vials containing 8 ml.—one average treatment course.

MULFORD COLLOID LABORATORIES

38th and Ludlow Streets, Philadelphia 4, Penna.

reprints and literature available **Reg. U. S. Pat. Off.*

1. Clin. Med. 2:1009, 1955.
2. Amer. Pract. & Digest Treat. 9:1447, 1956.
3. Clin. Med. 3:1059, 1956.
4. Amer. Pract. & Digest Treat. In press.
5. Files, Medical Department, Mulford Colloid Laboratories.

Heart Disease in Pregnancy

There is no evidence that pregnancy damages the heart or that the course of a rheumatic process is accelerated. Nor is there justification for discouraging pergnancy in cardiac patients on the ground that if the patient survives, life may be shortened. The apical diastolic murmur of mitral stenosis is usually intensified by pregnancy, and careful examination in the left decubitus position is essential before mitral stenosis can be excluded. Trial of mercurial diuretics should be used to confirm the suspicion of failure.

During pregnancy, Class I cardiac patients require no exercise restriction, but should take a one-hour rest during the day. Class II patients should refrain from heavy physical activity and have nine hours bed rest per night and a one hour rest during the day. Class III patients should refrain from even moderate exertion and have 10 hours bed rest per night and two hours rest each morning and afternoon. Class IV patients should remain at bed rest.

Normal delivery may be achieved with the use of forceps, but the patient should be watched carefully throughout the process. Cesarean section should not be done unless there is a clear indication for it.

Blood pressure, pulse and respiration should be taken hourly for 48 hours after delivery, and the physician notified at once of any unusual change. Unless the patient is dehydrated, 2 cc. of *Thiomerin* should be given subcutaneously at delivery and 24 hours later to minimize the danger of pulmonary edema. Bed rest except for passive leg exercises, and analgesics and sedatives for comfort, should be continued for not less than 48 hours in milder cases, for one week in more severe ones, and then gradually and cautiously relaxed. The great danger during this time is acute pulmonary edema and every effort should be made to prevent it.

From 95 to 98 per cent of pregnant cardiac patients can be carried successfully through pregnancy and labor on this regimen.

Janney, J. G., Jr., *Missouri Med.*, 55:25-30,1958.

Aortic Stenosis May Be of No Physiological Significance

Seven men, aged 51 to 67 years, were hospitalized with severe cardiac symptoms, including acute pulmonary edema in two, less acute heart failure in four, and intractable angina pectoris in one. All of them were thought to have aortic stenosis as an isolated valvular lesion possibly remediable by aortic valve surgery, but the clinical picture in each was in some way atypical. Catheterization of the left side of the heart was performed by right-sided posterior transthoracic puncture of the left atrium with the patient in the prone position and under local anesthesia—a barbiturate and meperidine were given as premedication. The catheterization established the correct diagnosis, *i.e.*, coronary artery disease with myocardial infarction in five patients, and mitral valve disease in two, thus preventing surgical intervention in these patients.

Patients with signs and symptoms suggestive of severe aortic stenosis may be suffering predominantly from coronary artery disease. Catheterization of the left side of the heart is indicated whenever surgery of aortic stenosis is under consideration.

Hancock, E. W., et al., *New England J. Med.*, 258: 305-312,1958.

briefs: THERAPEUTIC

The Anabolic Effects of Norethandrolone

Pharmacologic studies indicate that *Nilevar* possesses anabolic activity equivalent to testosterone propionate, with approximately one-sixteenth the androgenic activity. Eleven hospitalized gynecologic patients were kept on a constant diet and were given the drug in doses of 25 mg. intramuscularly 3 times a week for 10 weeks. All of the patients reported feeling more vigorous and experienced increased appetite. Weight changes were not determined as all patients were confined to bed. Three patients with cancer of the cervix required less narcotic medication during therapy. No changes indicating androgenic activity and no major side effects were observed.

Evidence of nitrogen retention appeared within a week after therapy was begun. The average percentage decrease in urinary nitrogen excretion for each patient ranged from 10 to 60 per cent. Sodium and potassium excretion levels in the urine did not vary. The response of the younger patients indicates that the drug exerts some direct effect on the Müllerian epithelium.

The synthetic steroid appears to exert a strong anabolic effect while displaying minimal androgenic activity. The lack of androgenicity in this compound is an important clinical advantage, particularly in the female patient.

Goldfarb, A. F., et al., *Obst. & Gynec.*, 11:454,1958.

Cobalt-Iron Therapy in Premature Infants

The newborn is subject to decrease in hemoglobin and red cell levels during the early part of the first year. An early phase of this anemia may occur within the first month or two of life, and may be due to failure of the bone marrow to assume full erythropoietic activity.

Iron deficiency anemia usually does not occur until the fourth to sixth month when reserve iron is exhausted. Rapid growth in the premature exaggerates iron deficiency. Prophylactic administration of iron is of little value during the early months of life, possibly due to the low level of erythropoiesis.

Cobalt has been shown to stimulate erythropoiesis, and erythropoietic activity appears to control iron absorption and utilization.

Of 44 premature infants, 16 received cobalt-iron therapy, 12 received ferrous sulfate, and 16 received no iron. The dosage of cobalt was 2 mg./kg./day of cobalt chloride. In both the cobalt-iron group and the plain iron group the daily dose of ferrous sulfate was 75 mg.

Treatment was continued for six months and hematologic determinations made at monthly intervals. There were no significant differences in the group treated with iron and the control group. The mean values obtained with cobalt-iron treatment, however, were above those in the other two.

At the two month period, the cobalt-iron group exceeded the other by more than 1 gm./100 cc. of hemoglobin.

During this interval, 15 cobalt-iron treated patients met or exceeded the mean value of the other groups. No intolerance, thyroid abnormality, or other untoward effects were seen. It appears that the low dosage of cobalt used in conjunction with iron is an effective prophylactic measure in the prevention of both the early anemia of infancy and the subsequent development of the iron deficiency state.

Diamond, E. F., et al., *Illinois M.J.*, 113:154,1958.

Treatment of Fat Embolism with Heparin

Three patients with fractures complicated by the occurrence of fat embolism were treated with heparin. The diagnosis in each case was made on clinical grounds only, but this was largely because it was considered to be so clear. The dosages of heparin employed were those used in deep-calf-vein thrombosis, and, although the records of clotting-time are not available, it was raised considerably in each case. Hemorrhage at the fracture site, delayed union, and more than usual joint stiffness after conventional treatment of the fracture were noted. The latter complication is possibly due to the forced neglect of physiotherapy in the early days after injury, when the general condition of the patient is so poor.

It is suggested that heparin treatment is worthy of further trial in this condition, and that a controlled series of cases would be justified.

Sage, R. H., & Tudor, R. W., *Brit. M.J.*, 1:1160-1161,1958.

The Use of Penicillin V in Private Pediatric Practice

The winter of 1956 and 1957 was marked by a large number of severe, acute infections of the throat clinically designated acute streptococcal pharyngitis. Throat cultures were obtained prior to starting medication in all cases. Follow-up cultures and clinical diagnoses were made in 24 hours. If the 24-hour culture was positive, or clinical improvement had not occurred, this was repeated in 72 hours. A total of 155 cultures were taken during the followup of the 74 patients. The dosage of penicillin V was 60,000 units (37.5 mg. per Kg. of weight per 24 hours) orally, in divided dosage at 4- to 8-hour intervals for a minimum of five days. A high incidence of acute glomerulonephritis was also observed. The age range was nine months to 12 years, duration of the illness prior to being seen, one to 72 hours.

Of the 74 patients, 28 (38%) had beta hemolytic streptococcal organisms isolated on the first culture—18 with another pathogen. Thirty-five (47%) had hemolytic staphylococcus aureus alone or with another pathogen, and 19 (26%) initial cultures grew out pneumococci. All the pure streptococcal cultures were negative in 24 hours. No cases of sensitivity were noted.

Most acute pharyngitis infections of bacterial etiology will respond satisfactorily to oral penicillin. This rapid clearing is considered important in the prevention of rheumatic fever and glomerulonephritis.

Parker, G. F., *J. Indiana M.A.*, 51:641-643,1958.

Buccally Administered Streptokinase

Antistreptokinase antibodies failed to increase in the serums of 14 patients during a four-week control period, but did increase and strengthen in 10 of the 14 a few weeks after buccal streptokinase therapy was begun. Since streptokinase is destroyed by gastric juice, the increase in antibodies could not follow unintentional ingestion. Elevated antithrombin levels were present in 23 of 27 serum determinations made in 14 patients receiving streptokinase buccally for periods varying from one day to four months. Higher values prevailed in the group receiving prolonged therapy.

There was evidence of anti-inflammatory effects. Many of the conditions treated had proved refractory to previous therapy, *e.g.*, patients with leg ulcer, bronchiectasis, chronic bronchitis and migratory phlebitis. Anti-inflammatory effects correlated well with elevation in serum antithrombin activity. Patients with acute thrombophlebitis showed rapid resolution of edema and cellulitis and when palpable the involved thrombotic venous segments appeared less tender, but were otherwise unchanged. Rapid thinning of previously thick, purulent, occasionally inspissated bronchial secretions occurred in patients with chronic bronchitis and bronchiectasis.

The buccal or sublingual route for administering streptokinase appears feasible. Enzyme therapy may now be used for long-term management of subacute or chronic bronchitis, bronchiectasis, retinal-vein thrombosis, indolent leg ulcer, acne and migratory phlebitis. Side effects are minimal.

Innerfield, I., et al., *New England J. Med.*, 258:1069-1074,1958.

Management of Ulcerative Colitis

The anatomical changes in ulcerative colitis can be visualized on proctoscopic and on x-ray examinations. About 90 per cent of such patients have visible changes in the rectum and rectosigmoid.

The range of severity is wide, from the mild proctitis to the severe illness.

Treatment is largely by diet, sedation, vitamin therapy, antibiotics or sulfonamide drugs, and the use of transfusions. The majority of patients on such a regimen will have symptomatic remission. Steroids are available for the sicker patients.

Some 95 per cent of patients with chronic ulcerative colitis, after periods of remission have had recurrence of symptoms. Patients with proctitis are seldom incapacitated and are easy to manage. In a group of 20 patients with fulminating disease and a high, continuous fever for over two weeks, only four remained under medical treatment. The others were either operated on, or have died. It is believed that early surgery should be seriously considered more often in these circumstances.

The patient with less severe but incapacitating symptoms which last for long periods of time is also difficult to manage. The patient who has continuing diarrhea, with six to ten stools a day for several months, who does not respond to simple supportive treatment, often seeks help elsewhere. In this group it is difficult to set down any rules of action. Patients who have less severe symptoms may do well under steroid therapy.

Experience with steroids given to patients who have failed to respond to simpler measures, indicates that half of these patients respond in terms of disappearance of constitutional symptoms, control of the diarrhea, increased sense of well being and improved nutrition. It is not believed that the use of steroids has modified the long-term course of the disease. It is clear that this therapy is of value in the immediate relief of the severely ill in some instances. When the patient is on steroid therapy, perforation may occur and not be recognized. It may be extremely difficult to estimate the severity of the disease in patients under steroid therapy. It may be advisable, with seriously ill patients, to withhold steroid therapy in order to establish whether or not surgical intervention is warranted.

The majority of patients will have symptomatic remission under treatment with available medical measures. Some 20 per cent will need surgery.

Flood, C. A., et al., *Bull. New York Acad. Med.*, 34:366-386,1958.

My formula for reinforcing primary therapy is VITERRA®

the *comprehensive* nutritional supplement

In some 3 out of 4 of the patients you'll see this week, nutrition is a factor in the delicate balance between relapse and recovery.

If you back up your primary therapy with VITERRA, it will help increase the chances of therapeutic success. That's because VITERRA meets the demands of stress with both vitamins *and* minerals. You have your choice of three dosage forms: Capsules, VITERRA THERAPEUTIC (for high potencies), and VITERRA TASTITABS® (deliciously ideal for children).

Dosage: **usually one capsule daily.**

Supplied: **bottles of 30 and 100. VITERRA TASTITABS,® bottles of 100 and 250; VITERRA THERAPEUTIC,® bottles of 30 and 100.**

Each VITERRA Capsule contains:

Vitamins	
Vitamin A (Palmitate)	5,000 U.S.P. Units
Vitamin D (Irradiated Ergosterol)	500 U.S.P. Units
Vitamin B_{12} U.S.P.	1 mcg.
Thiamine Hydrochloride U.S.P.	3 mg.
Riboflavin U.S.P.	3 mg.
Pyridoxine Hydrochloride U.S.P.	0.5 mg.
Niacinamide U.S.P.	25 mg.
Ascorbic Acid U.S.P.	50 mg.
Calcium Pantothenate	5 mg.
Vitamin E (from mixed tocopherols concentrate)	3.7 I.U.
Minerals	
Calcium (from Dicalcium Phosphate)	213 mg.
Cobalt (from Cobaltous Sulfate)	0.1 mg.
Copper (from Cupric Sulfate)	1 mg.
Iodine (from Potassium Iodide)	0.15 mg.
Iron (from Ferrous Sulfate)	10 mg.
Manganese (from Manganous Sulfate)	1 mg.
Molybdenum (from Sodium Molybdate)	0.2 mg.
Phosphorus (from Dicalcium Phosphate)	165 mg.
Potassium (from Potassium Sulfate)	5 mg.
Zinc (from Zinc Sulfate)	1.2 mg.

Psychosurgery: Indications and Prospects

Today psychosurgery is overshadowed by the tranquilizers and euphorians. In 1949, when lobotomy was at its peak, only 6.5 per 1,000 patients in mental hospitals were treated with these drugs. During the 10- to 20-year postlobotomy period, 70 per cent of the patients were out of the hospital and 50 per cent of all survivors were employed or keeping house. By 1949 prefrontal lobotomy had given place to transorbital lobotomy and other selective operations, since the latter were found to be less damaging to the personality and equally effective therapeutically.

In studies of patients receiving tranquilizer therapy, lessened response to external and internal stresses have been noted, with greater tolerance to frustration, lessened tension and anxiety, better relaxation and improved habits — results similar to those achieved by lobotomy. Yet patients receiving drug therapy are more aware of themselves, more self-conscious than those who have had lobotomy.

While lobotomy and similar operations may produce occasional brilliant results in chronic schizophrenic patients, they are devastating to better preserved patients. Limiting the operation's extent and avoiding trauma to the cortex with its consequent danger of convulsive seizures, have made lobotomy relatively safe. Observance of the proper indications, and the proper timing of operations, have made it possible to return some 80 per cent of patients with a fixed state of tortured self-concern to a more cheerful and effective existence. When a patient is operated upon by one of the selective methods before deterioration has set in, the only personality changes appear on the positive side. With the present methods, such a rate of success cannot be attained in chronic patients in state hospitals. Psychosurgery may be on the threshold of another advance that will bring another host of patients to better health.

Since the brain of a schizophrenic patient shows nothing pathologic macroscopically or microscopically, even after decades of the psychosis, and since occasionally a patient returns to normality after years of confinement, and without any treatment, there is hope for the schizophrenic. Ataractics for overactivity and anxiety, euphoriants and electroshock for depression, lobotomy for obsessive tension, and mixtures of these treatments for syndromes that show various combinations, will enable the psychiatrist to treat effectively a large number of patients.

The symptom that is least responsive to any of these treatments is hallucination. Practically all schizophrenic patients unimproved or relapsing

after lobotomy are hallucinating. Drugs and shock therapy are beneficial in early cases, but there is no good evidence that these phenomena are abolished in long-standing cases. The case in which extensive prefrontal lobotomy succeeds after failure of transorbital or rostral lobotomy are mostly those with hallucinations. The apparent difference between the two methods lies in the severing of connections between the frontal and temporal lobes.

Freeman, W., *California Med.*, 88:429-434,1958.

Rib Fractures and Complications

Usually the "broken" rib will heal with or without treatment. Treatment is directed toward the maintenance or restoration of normal breathing capacity. Intercostal nerve block is the best form of treatment of rib fractures, for with the relief from pain, normal breathing capacity and normal cough reflex are restored.

The block of the nerves of fractured ribs plus the two above and below the fractures is made, using procaine hydrochloride solution, 0.5 or 1.0%. Skin wheals are placed 3 cm. laterally to the spinous processes at the proper levels. In obese patients it may be necessary to probe to the rib and then direct the needle downward to slide it beneath the lower rib border and inward into the intercostal space. Relief from pain is rapid and usually one block is sufficient. If the pain recurs, the block should be repeated.

In every case of rib fracture atelectasis, pulmonary concussion, pneumothorax, subcutaneous emphysema, hemothorax, and paradoxical respiration should be considered.

Crowley, D. F., Jr., *J. Iowa M. Soc.*, 48:244-250,1958.

Diagnosis and Therapy of the Commonest Anemia

Microcytic hypochromic anemia will respond to iron. Iron deficiency results from chronic blood loss in the adult, or a diet inadequate in iron salts in the growing child. Careful scrutiny for chronic bleeding is mandatory.

Oral administration of ferrous salts is the preferred treatment in all but a small percentage of patients. One individual may absorb 5 to 15 per cent of ferrous iron and 2 to 10 per cent of ferric iron salts when ingested in quantities up to 100 mg. per day. When iron deficiency exists, absorption is probably increased considerably; 10- to 20-fold increase results from the simultaneous administration of ascorbic acid.

Ferrous sulfate, 1 gm. per day, will supply 200 mg. of elemental iron, of which at least 20 mg. will be absorbed. A schedule such as 330 mg. of ferrous sulfate given after each meal, with 50 to 100 mg. of ascorbic acid, is frequently employed. The higher cost of "shotgun" preparations and the usually smaller doses of elemental iron are disadvantageous. Gastric irritation, diarrhea, or constipation, which develop in some patients on iron therapy, are often avoided by smaller doses at the onset, increased to full dosage within a week or two.

For infants, iron ammonium citrate in water and glycerin is employed, 200 mg. three times each day. At one year two or three times this dose is given. When oral administration is impracticable in the infant, the intramuscular injection of *Imferon* is of value. One cc. contains 50 mg. of elemental iron which, when injected deep into the muscle, is apparently free of adverse side-reactions. Since practically no iron is lost from the body once it enters the tissues, except through blood loss, the parenteral administration of excesses of iron over long periods will lead to tremendous iron concentrations in the body, and conceivably to diffuse tissue injury. Simple charts are available for the determination of the correct dose of iron given parenterally. They relate total dose of iron to the weight of the patient and his initial hemoglobin concentration.

Saccharated iron oxide is given intravenously, diluted in saline solution, 50 to 100 mg. per injection to adults, smaller amounts to children. Though more effective and less toxic than earlier preparations for such use, extreme care must be used with each administration. In an adult indications include a malabsorption syndrome making oral therapy ineffective, and extreme sensitivity of the gastrointestinal tract to iron salts.

Lichtman, H. C., *J.A.M.A.*, 167:735-741,1958.

Idiopathic Pneumoperitoneum

Free air found in the peritoneum may be due to "Forme frusté" ulcerations in the gastrointestinal tract, lower-lobe pneumonia and emphysema with blebs adherent to the diaphragm, negative intraperitoneal pressure sucking air into the peritoneum through the Fallopian tubes (especially in the postpartum patient), rupture of intestinal wall cysts. These patients often complain of chest pain, though they appear well, and give a history of epigastric distress. The diagnosis is made by x-ray film of the chest. Only conservative treatment is indicated.

Durant, J. R., *Connecticut M.J.*, 22:282-285,1958.

Complete Intrathoracic Goiter Simulating an Aneurysm of the Ascending Aorta

Aberrant thyroid tissue is most commonly found in the thorax. Many case reports have been published about aberrant thyroid tissue, whereas reports of complete intrathoracic goiters without visible cervical connections are rare.

A case of complete intrathoracic goiter without visible connection with the neck is of interest because of the difficulty in differential diagnosis despite radioactive iodine studies and angiocardiography. The angiocardiographic result can be explained on the basis of the vacsularity of the tumor, which took up contrast material in high concentration directly from the aorta and resulted in the impression of "a small saccular aneurysm." Despite these studies, operation was necessary to make the diagnosis and remove the tumor.

Codington, J. B., & Cowley, R. A., *J.A.M.A.*, 167: 461-462,1958.

Paper Strip Test For Proteinuria

A new test for proteinuria employs impregnated paper sticks (*Albustix*) which remain yellow when dipped in normal urine but become green or blue if the urine contains protein. The strips contain citrate buffer, pH 3, and an indicator, tetrabromphenol blue.

Albustix is a simple and speedy test for proteinuria, and although less sensitive than other tests for urine protein, it appears to be an adequate screening test. Variation of urine acidity or alkalinity within physiological limits does not interfere with the results qualitatively, but it slightly affects the quantitative indication. Gross alkaline fermentation of urine can lead to spurious positive indications, while the addition of acid or toluene as preservatives can lead to false-negative reactions.

Frazier, S. C., *Brit. M.J.*, 1:981-983,1958.

Testicular Tumors in the Newborn

Two of eight cases of testicular tumor in newborn infants were highly malignant, three were potentially malignant, and three were benign. The differential diagnosis between torsion and tumor cannot be made on the basis of physical examination since both are firm, painless swellings in the scrotum which cannot be transilluminated. Any infant with such a scrotal swelling should be explored without delay and orchiectomy should be performed. Unless it is, the risk of postoperative infection in such a culture medium, of missing a hidden malignant tumor, or of increasing the possibility of later malignancy in an atrophic testis is present. The infants withstand such an operation extremely well.

Smith, A. M., & Riese, K. T., *Connecticut M.J.*, 22:180-183,1958.

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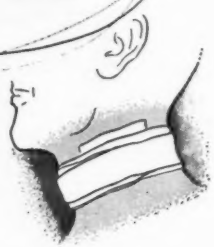

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Intraperitoneal Blood Transfusions in Children

Introduction of sterile citrated blood into a healthy peritoneal cavity has been found to be of value in raising the hemoglobin and red-cell content of the circulating blood. The major advantage of such a transfusion is the ease of administration, a point of considerable importance when dealing with infants and young children. However, intravenous transfusions in infants can be fatal due to overloading of the circulation.

Intraperitoneal transfusions of whole citrated blood were given to 23 anemic children, one month to four years of age. There was nutritional anemia in two cases, nutritional anemia with infection in six, chronic infection in two, sickle-cell anemia in two, sickle-cell anemia with acute infection in five, malaria in five, and ankylostomiasis in one.

The blood of the donor and that of the recipient were grouped and cross-matched for compatibility in all cases. Standard M.R.C. type bottle and transfusion sets were used with a short-bevelled wide-bore needle. Preliminary sedation was not given as a routine since many of the children were moribund and collapsed at the time of transfusion. In less severe cases where the child was apprehensive or irritable, chloral hydrate was given one hour before transfusion.

The injection was made one inch above the umbilicus after careful cleansing of the abdominal skin. To control the depth of penetration of the needle the skin was grasped between thumb and forefinger of the left hand and traction exerted on it while the needle was pushed slowly and firmly into the peritoneal cavity with the right hand. Immediately the needle had penetrated the skin, the control clip on the giving-set was opened fully and the previously warmed blood was allowed to run in steadily. In all cases the transfusion was completed within 10-20 minutes. The amount of blood at any one time varied from 60 to 300 ml., the average was 23 ml. per Kg. of body weight. At the completion of the transfusion the foot of the cot was raised on blocks to encourage drainage of the blood towards the diaphragm.

Of the 23 cases, 14 babies survived. The rate of hemoglobin response varied considerably without regard to the amount of blood given. Eight cases showed a steady rise after a single transfusion. There was no significantly better response in the three who received more than one transfusion. In all cases, a rise in hemoglobin was obtained in 24 hours.

Four children showed restlessness and abdominal discomfort after receiving amounts of blood in excess of 100 ml. Two vomited at the completion of the transfusion, one had a fe-

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Mildy confused senile patients may be rehabilitated from public and private institutions and cared for in the home by sustained treatment with the NICOZOL formula.[1,2,3]

1. Levy, S., *J.A.M.A.*,153:1260,1953
2. Thompson L., Procter, R., *North Carolina M. J.*, 15:596,1954
3. Thompson, L., Procter, R., *Clin. Med.* 3:325,1956

NICOZOL is supplied in capsule and elixir forms. Each capsule or ½ teaspoonful contains:
Pentylenetetrazol.....100 mg.
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Optimum Age for Surgical Closure of Patent Ductus Arteriosus

Surgical closure of a patient ductus arteriosus should be carried out on any child who shows symptoms as early as the diagnosis is established, and in asymptomatic patients before they reach the age of five years. The operative morbidity and mortality in infants and younger children is no greater than that experienced in older children. Neglect or failure to effect closure in early life may expose the infant with symptoms to progressive myocardial decompensation and the young child to the needless threat of cardio-respiratory disability, growth failure not entirely reversible, and to such additional serious complications as endarteritis, irreversible pulmonary hypertension, and degenerative disease of the major and minor pulmonary vessels.

Clatworthy, H. W., Jr., & McDonald, V. G., Jr., *J.A.M.A.*, 167:444-447,1958.

Feeding of Infants and Children in Hot Weather

Hot weather imposes no special dietary requirements for healthy infants and children, except for an increased water intake. If infants and children taking well-balanced diets do not tolerate ordinary heat stress, they should be investigated for illness. Poor appetites and faulty eating habits may result from the uncontrolled use of cold, high-calorie drinks or foods, from failure to take adequate outdoor exercise, or from overindulgence in between-meal snacks. It is unwise for adults to "condition" children to dislike hot weather or to foist summertime food fads on them.

Norman, F. A., & Pratt, E. L., *J.A.M.A.*, 166:2168-2170,1958.

brile reaction of 100° following each transfusion, and one had a prolonged febrile illness, the origin of which is unknown.

Intraperitoneal blood transfusions have a definite value in the treatment of the anemias of children. In cases of hemorrhage, the necessity for rapid replacement still requires the intravenous route.

Macdougall, L. G., *Brit. M.J.*, 1:139-142,1958.

Multiple Causes of Iron Deficiency in Infants

The most significant predisposing factors found in 272 cases of hypochromic anemia were low birth weight, high birth order, twinning, and masculinity. The poor diets eaten by these infants are similar to those of a much larger number of infants who did not develop anemia of the same severity.

A birth weight of less than 3 kg. (6.5 lb.) is the most common predisposing factor. Prematurity was a factor in 80 per cent of the patients with a hemoglobin of less than 5 gm. per 100 cc. Reduction of the iron supplies at birth may be due to maternal iron deficiency or fetal blood loss. Perinatal hemorrhage may explain the high incidence of hypochromic anemia in twins. The more frequent occurrence of hypochromic anemia in male infants is a reflection of their relative immaturity and increased growth rate.

The prevention of hypochromic anemia depends largely on the recognition of susceptible infants. This group should be given adequate doses of medicinal iron prophylactically, and should be carefully watched for the development of anemia.

Woodruff, C. W., *J.A.M.A.*, 167:715-720,1958.

The Psychology of Medical Practice

by Marc H. Hollender, M.D., State University of New York. W. B. Saunders Company, Philadelphia & London. 1958. $6.50

There are chapters on the doctor-patient relationship, the medical patient, the surgical patient, the patient with carcinoma, the obstetrical patient, the pediatric patient in health and in illness. Then there is one on psychological considerations in medication, and one on the non-medical prescription. It is a large subject dealing with matters on which opinions will differ widely. It seems that the psychiatric aspect is given too large a part in the total consideration.

Correlative Neuroanatomy and Functional Neurology

by Joseph G. Chusid, M.D., St. Vincent's Hospital, New York; and Joseph J. McDonald, M.D., American University of Beirut, Beirut, Lebanon. Ninth Edition. Lange Medical Publications, Los Altos, Calif. 1958. $4.50

It would seem the book's declared purpose as being for the beginner in neurology to serve as a supplement to standard text and to serve physicians preparing for specialty board examinations has been amply met.

A Short History of Anatomy and Physiology From The Greeks to Harvey

by Charles Singer. Dover Publications, Inc., New York. 1957. $1.75

There is much of entertainment in the story. The reviewer was somewhat disappointed not to find corroboration of the tale that early anatomists depicted males as having only 11 ribs on one side, females as having 12 each side—the loss of one of Adam's ribs in the making of Eve being perpetuated in the male line of descent.

Modern Clinical Psychiatry

by Arthur P. Noyes, M.D., Norristown State Hospital, Norristown, Pennsylvania; and Lawrence C. Kolb, M.D., Columbia University. Fifth Edition. W. B. Saunders Company, Philadelphia & London. 1958. $8.00

It is stated that "it has been our purpose, so far as facts and experience seem to warrant, to maintain a dynamic and developmental orientation in the discussion of the various personality disorders that constitute the thesis of psychiatry." So far as this reviewer understands this declaration of purpose, he may say that he believes the purpose has been fairly achieved.

Crime and Insanity

edited by Richard W. Nice. Philosophical Library, New York, N.Y. 1958. $6.00

The question of what degree of mental capacity should be accepted for holding a man accountable for his unlawful acts has agitated the minds of thoughtful men throughout recorded time. Whether or not any person could have acted other than as he did at any certain time is open to doubt. Many of the wisest of mankind have accepted the belief that justice is nothing more nor less than a large expediency. That man of "much learning," the Apostle to the Gentiles, reminded "all things are lawful but all things are not expedient." You may be entertained by the book, may even be instructed.

Principles of Internal Medicine

Editors T. R. Harrison, Raymond D. Adams, Ivan L. Bennett, Jr., William H. Resnik, George W. Thorn and M. M. Wintrobe. Third Edition. McGraw-Hill Book Company, Inc., The Blakiston Division, New York, Toronto, & London. 1958. $18.50

We are all familiar with books on Principles of Surgery. Few of us had ever seen a book on Principles of Internal Medicine until the first edition of the work under review appeared. The declaration in the first edition of a purpose "to provide for the medical student a certain unity between reading and instruction" in a text "which presents internal medicine in the way that the subject is approached in the curriculum" had great appeal for the thoughtful medical man. For this edition the book has been reset and its organization modified. The book discusses The Physician and the Patient, Cardinal Manifestations of Disease, Biologic Considerations, Metabolic and Endocrine Disorders, Disorders Due to Chemical and Physical Agents, Diseases Due to Biologic Agents, Diseases Associated with Reactions to Stress and to Antigenic Substances, Diseases of Organ Systems and Care of the Patient.

This reviewer agrees with the editors that discussion of the main symptoms and of their mechanism is useful to the physician who thinks of specific diseases only after he has taken a good history and elicited and interpreted the patient's symptoms. He goes further in saying that this is the most useful way of arriving at a proper diagnosis and prescribing the best treatment.

An appendix devoted to Laboratory Values of Clinical Importance is a fitting end to a satisfying text on internal medicine.

How to Live With Diabetes

by Henry Dolger, M.D., Mt. Sinai Hospital, New York; and Bernard Seeman. W. W. Norton & Company, Inc., New York, N.Y. 1958. $3.50

The name is well chosen and the text is worthy of the name. In choosing a book for his diabetic patients a doctor need go no further.

The Medical World of The Eighteenth Century

by Lester S. King, M.D., The University of Chicago Press, Chicago, Ill. 1958. $5.75

An entertaining and elaborate discussion of the subject on a basis of broad knowledge and a fitting sense of humor.

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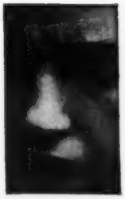
of **danger signals**
in office practice



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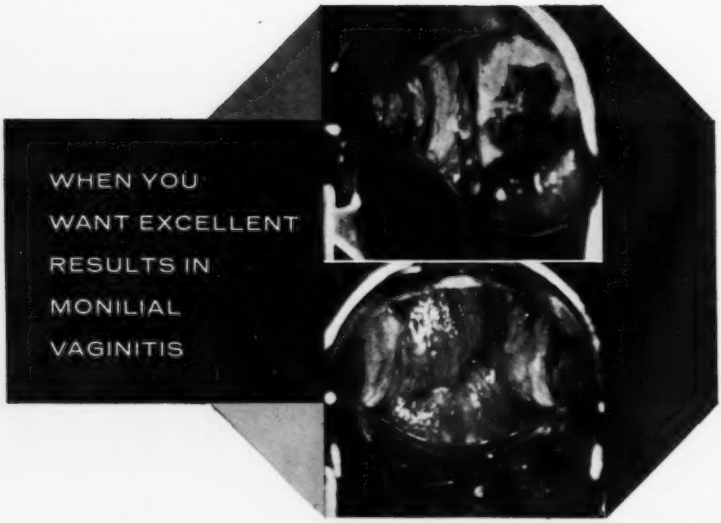

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1. Thomas, H. H.: Obstet. & Gynec. 9:163, 1957. 2. Browne, A. D. H.: J. Irish M.A. 40:86, 1957. 3. Pace, H. R., and Schantz, S. I.: J.A.M.A. 162:268, 1956.

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Anomalies of Infants and Children

by D. McCullagh Mayer, D.D.S., M.D., F.A.C.S., F.I.C.S., New York Medical College; and Wilson A. Swanke M.D., F.A.C.S., F.I.C.S., Ankara University, Turkey. McGraw-Hill Book Company, Inc., The Blakiston Division, New York, Toronto, & London. 1958. $12.00

It is claimed that here, in one volume, are presented the etiology, diagnosis, prognosis, time and type of treatment for the more common congenital and acquired malformations. One may well allow the claim as justified.

Skin Grafting

by James Barrett Brown, M.D., Washington University School of Medicine; and Frank McDowell, M.D., Washington University School of Medicine. Third edition, with 328 figures and 6 color plates. J. B. Lippincott Company, Philadelphia & Montreal. 1958. $15.00

Since most skin grafting is done for burns, they are elaborately considered as to prevention, incidence, management and mortality. The chapters on the early general and local care of burns are of value to the general practitioner. Those chapters on preparation for and performance of skin grafting cover management at the hands of the specialist. All the different forms of grafts and flaps are described, and their fields of usefulness defined. Prevention of contraction, special features of repairs of different anatomic parts, the hands, the body, the genitalia, the thighs and legs, the face, the ears, all are covered in great detail. There are chapters on restoration of defects from removal of tumors, from various injuries, repair of electrical and cathode-ray burns, of radiation injuries and atomic burns, on skin grafting in military surgery, and two chapters of special interest deal with faults of skin grafts and discuss final results. The illustrations are ample and supplement the text to make the whole a book of rare excellence.

Orthopedic Diseases: Physiology—Pathology—Radiology

by Ernest Aegerter, M.D., Temple University; and John A. Kirkpatrick, Jr., M.D., Temple University Medical Center, Philadelphia. W. B. Saunders Company, Philadelphia & London. 1958. $12.50

This book is put out "as a starter." It discusses bone disease from the viewpoint of altered anatomy and physiology and tries to interpret it in terms of symptoms and physical findings including x-ray pictures. The virtue claimed is that the volume makes available an abundance of valuable material selected by the authors over a period of 20 years. On the foundation of elementary consideration is erected a structure of great practicality.

Medical Electrical Equipment

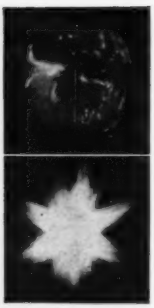
Advisory Editor Robert E. Molloy, M.B., F.F.A., R.C.S., Philosophical Library, Inc., New York, N.Y. 1958. $15.00

This reviewer's knowledge of this subject is too meager to allow of an expression of opinion on his own. He accepts the standing of the makers of the work as amply attesting its reliability.

in vaginal trichomoniasis—

explosion

is the solution



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VAGISEC therapy relieved half the patients of all annoying symptoms of trichomoniasis after only one week of treatment. In agreement with findings of other investigators,[2,3] three to four weeks of therapy were sufficient in most cases for complete eradication of trichomonads.

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References: 1. Weiner, H. H.: Clin. Med. *5*:25 (Jan.) 1958. 2. Decker, A.: New York J. Med. *57*:2237 (July 1) 1957. 3. Davis, C. H.: West. J. Surg. *63*:53 (Feb.) 1955.

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